

Title of Each Class of Securities to Be Registered	Proposed Maximum Aggregate Offering Price ⁽¹⁾	Amount of Registration Fee ⁽²⁾
Common stock, par value \$0.001 per share	\$86,250,000	\$10,453.50

- (1) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(o) under the Securities Act of 1933, as amended.
- (2) Calculated pursuant to Rule 457(o) based on an estimate of the proposed maximum aggregate offering price.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

The information in this preliminary prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell these securities and we are not soliciting offers to buy these securities in any state or other jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED JUNE 21, 2019

PRELIMINARY PROSPECTUS

Shares



Common Stock

This is an initial public offering of common stock by Fulcrum Therapeutics, Inc. We are selling _____ shares of common stock. The estimated initial public offering price is between \$ _____ and \$ _____ per share.

Prior to this offering, there has been no public market for our common stock. We have applied to list our common stock on the Nasdaq Global Market under the symbol "FULC."

We are an emerging growth company as that term is used in the Jumpstart Our Business Startups Act of 2012 and, as such, have elected to comply with certain reduced public company reporting requirements for this prospectus and future filings.

	<u>Per Share</u>	<u>Total</u>
Initial public offering price	\$ _____	\$ _____
Underwriting discounts and commissions ⁽¹⁾	\$ _____	\$ _____
Proceeds to Fulcrum, before expenses	\$ _____	\$ _____

(1) We have agreed to reimburse the underwriters for certain FINRA-related expenses. See "Underwriters" on page 196.

We have granted the underwriters the right to purchase up to an additional _____ shares of common stock. The underwriters may exercise this right at any time within 30 days after the date of this prospectus.

Investing in our common stock involves risks. See "Risk Factors" beginning on page 10 of this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares of common stock to purchasers on or about _____, 2019.

MORGAN STANLEY

BofA MERRILL LYNCH

SVB LEERINK

_____, 2019

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Neither we nor the underwriters have authorized anyone to provide you with any information other than that contained in this prospectus, any amendment or supplement to this prospectus or in any free writing prospectus we may authorize to be delivered or made available to you. We and the underwriters take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or any sale of shares of our common stock. Our business, financial condition, results of operations and prospects may have changed since that date.

For investors outside the United States: we have not, and the underwriters have not, done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus outside the United States.

Trademarks, service marks and trade names appearing in this prospectus are the property of their respective owners. Solely for convenience, some of the trademarks, service marks and trade names referred to in this prospectus are listed without the ® and ™ symbols.

PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus and does not contain all of the information that you should consider in making your investment decision. Before investing in our common stock, you should carefully read this entire prospectus, including our consolidated financial statements and the related notes thereto and the information set forth in the sections titled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations." Unless the context otherwise requires, we use the terms "company," "we," "us" and "our" in this prospectus to refer to Fulcrum Therapeutics, Inc.

Overview

We are a clinical-stage biopharmaceutical company focused on improving the lives of patients with genetically defined diseases in areas of high unmet medical need, with an initial focus on rare diseases. We have developed a proprietary product engine that we employ to systematically identify and validate cellular drug targets that can potentially modulate gene expression to treat the known root cause of genetically defined diseases. We are using our product engine to identify targets that can be drugged by small molecules regardless of the particular underlying mechanism of gene mis-expression. We have identified drug targets to treat the root causes of facioscapulohumeral muscular dystrophy, or FSHD, and certain hemoglobinopathies, namely sickle cell disease, or SCD, and β -thalassemia. We expect to initiate a Phase 2b clinical trial of losmapimod, our product candidate for FSHD, in mid-2019. We commenced a Phase 1 clinical trial in February 2019 to obtain safety and tolerability data for losmapimod in patients with FSHD. We plan to submit an investigational new drug application, or IND, for FTX-HbF, our product candidate for certain hemoglobinopathies, in mid-2020.

We are using our proprietary product engine to identify and validate drug targets and develop product candidates to address diseases caused by the mis-expression of certain genes. Our product engine integrates patient-derived tissue-relevant cell models and drug target screens with our pharmacologically-diverse small molecule compound library and customized CRISPR libraries. We also employ computational biology and FulcrumSeek, our proprietary relational database, to guide target selection and to generate hypotheses on other targets that might be relevant along a gene regulatory pathway.

Our first product candidate, losmapimod, is a small molecule that we are developing for the treatment of FSHD, a rare, progressive and disabling muscle wasting disorder that leads to significant physical impairments and disability. Losmapimod selectively targets p38a/b mitogen activated protein kinase, or p38a/b. We utilized our product engine to discover that inhibition of p38a/b reduced expression of the *DUX4* gene in muscle cells derived from patients with FSHD. The mis-expression of the *DUX4* gene is the known root cause of FSHD. There are no approved therapies for FSHD, one of the most common forms of muscular dystrophy, with an estimated patient population of 16,000 to 38,000 in the United States.

Following our discovery of the role of p38a/b inhibitors in the reduction of *DUX4* expression, we performed an extensive review of known compounds. As a result of our evaluation, we identified losmapimod as the preferred developmental candidate based on the substantial and attractive preclinical and clinical data. We in-licensed losmapimod from affiliates of GlaxoSmithKline, or GSK, in February 2019 and received active pharmaceutical ingredient and losmapimod tablets that had been manufactured by GSK. GSK had previously treated nearly 3,500 subjects with losmapimod across multiple clinical trials, including one Phase 3 clinical trial. GSK did not conduct a clinical trial of losmapimod in patients with FSHD or any other muscle disorder. We have conducted extensive preclinical testing of losmapimod in patient-derived tissue-relevant cell models and have observed that losmapimod selectively reduced *DUX4*-driven gene expression and restored a healthy gene expression signature with minimal impact on healthy human muscle cells or other cell types.

We plan to conduct a randomized, double-blind placebo-controlled Phase 2b clinical trial to investigate whether treatment with losmapimod reduces *DUX4*-driven gene expression in affected skeletal

muscle. In this Phase 2b clinical trial, we will also evaluate the safety and tolerability of losmapimod. We plan to concurrently conduct an open label Phase 2 clinical trial to investigate the safety and tolerability of chronic treatment with losmapimod in patients with FSHD. In this open label trial, we will also evaluate the ability of losmapimod to reduce DUX4-driven gene expression in affected skeletal muscle over varying treatment durations. We expect to initiate the Phase 2b clinical trial at multiple sites in the United States and Europe and the open label Phase 2 clinical trial in Europe in mid-2019. We expect to complete a Phase 1 clinical trial in healthy volunteers and patients with FSHD in 2019. We utilized data from GSK's clinical trials of losmapimod and our preclinical data to submit in May 2019 an IND, and clinical trial applications, or CTAs, in Europe and Canada, that will enable us to advance our clinical development plan for losmapimod in FSHD, including initiating a Phase 2b clinical trial in mid-2019. The FDA accepted the IND in June 2019. The timing of the initiation of the Phase 2b clinical trial is not dependent on the completion of the Phase 1 clinical trial.

We are additionally conducting several preparatory studies to assess biomarker endpoints and clinical outcome assessments and are participating in a natural history study that will follow 150 subjects with FSHD in the United States and 70 subjects in Europe over 18 months. We expect to utilize the data generated from our preparatory studies and the natural history study to inform future clinical trial designs and discussions with regulatory agencies. We believe that these preparatory studies and the safety data from GSK's prior losmapimod clinical trials, together with safety and efficacy data generated from our Phase 1 and Phase 2 clinical trials, may enable us to apply for accelerated approval of losmapimod for the treatment of FSHD. If we observe positive results in our Phase 2b clinical trial based on our proposed biomarker efficacy endpoint of measuring DUX4-driven gene expression in muscle biopsies, we plan to discuss accelerated approval with regulatory agencies and may seek accelerated approval if such regulatory agencies agree that our biomarker endpoint is sufficiently predictive of clinical benefit. The FDA or other regulatory authorities may require us to conduct comparability assessments of GSK-manufactured tablets to tablets manufactured by us or another party.

Our second product candidate, FTX-HbF, is a small molecule designed to upregulate fetal hemoglobin in patients with SCD and b-thalassemia. SCD is a genetic blood disorder caused by a mutation in the b-subunit gene, or *HBB* gene. This mutation results in the formation of abnormal hemoglobin, which causes red blood cells, or RBCs, to change from a round shape into a sickle shape that significantly impairs their function. b-thalassemia is a rare blood disorder caused by various genetic mutations in the *HBB* gene that can significantly impair the production of RBCs.

We designed FTX-HbF to compensate for the root cause of these hemoglobinopathies by inducing the expression of the two g-globin genes, *HBG1/2*, whose expression is normally silenced shortly after birth. The *HBG1/2* genes encode for g-globin, a component of fetal hemoglobin, which is known to compensate for the presence of abnormal hemoglobin in SCD and b-thalassemia. We have observed *in vitro* and *in vivo* activation of the *HBG1/2* genes in preclinical studies with FTX-HbF. We have also observed that FTX-HbF demonstrated robust levels of fetal hemoglobin elevation with no adverse effect on important cellular health markers. We have initiated IND-enabling studies and plan to submit an IND for FTX-HbF in mid-2020.

According to the National Institutes of Health, or NIH, there are approximately 7,000 rare, genetically defined human diseases, many of which have inadequate or no approved treatments. We plan to utilize our product engine to complete four new drug target identification screens in 2019 in Duchenne muscular dystrophy, Friedreich ataxia, myotonic dystrophy 1 and a-synucleinopathies. We also expect to complete an additional six screens in 2020. Our current drug target identification and development efforts are focused on rare neuromuscular disorders, hemoglobinopathies and central nervous system, or CNS, diseases. We also anticipate utilizing our product engine to discover drug targets for genetically defined diseases in other therapeutic areas. In addition to drug targets that we prioritize for internal development, we may identify other drug targets that we would consider for development through partnerships.

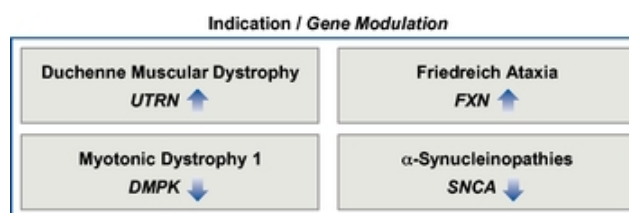
Our Pipeline

We designed our proprietary product engine with potential application across a broad array of genetically defined diseases with a known root cause. The following chart summarizes key information about our lead product candidates.



Our Discovery Screening Programs

We are leveraging the broad applicability of our product engine to discover drug targets for other rare, genetically defined neuromuscular and CNS diseases. We plan to complete four additional screens in 2019, seeking to identify and validate drug targets that can potentially modulate gene expression to address the root causes of Duchenne muscular dystrophy (*UTRN* gene), Friedreich ataxia (*FXN* gene), Myotonic dystrophy 1 (*DMPK* gene) and α-Synucleinopathies (*SNCA* gene).



Our Strategy

We are leveraging the broad applicability of our proprietary product engine to discover and develop small molecule therapies that modulate gene expression to address the known root cause of genetically defined diseases in areas of high unmet medical need, with an initial focus on rare diseases. We believe that our initial product candidates for the treatment of FSHD, SCD and β-thalassemia may have the potential to treat patients with these debilitating and, in some cases, life-threatening illnesses. The key components of our strategy include:

- Rapidly develop losmapimod for the treatment of FSHD.
- Advance FTX-HbF into clinical development.
- Continue to apply our proprietary product engine to grow our portfolio of product candidates for the treatment of genetically defined diseases.
- Further expand our product engine capabilities.
- Maximize the commercial potential of our product candidates.
- Selectively enter into strategic partnerships to maximize the value of our product engine and pipeline.

Risks Associated with Our Business

Our business is subject to a number of risks of which you should be aware before making an investment decision. These risks are discussed more fully in the "Risk Factors" section of this prospectus. These risks include, but are not limited to, the following:

- We have incurred significant losses since our inception. We expect to incur losses over the next several years and may never achieve or maintain profitability. As of March 31, 2019, we had an accumulated deficit of \$105.0 million.
- We will need substantial additional funding. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.
- Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.
- We have identified conditions and events, namely our need to raise additional capital, that raise substantial doubt about our ability to continue as a going concern, and our independent registered public accounting firm's report on our consolidated financial statements appearing at the end of this prospectus includes a going concern uncertainty paragraph.
- We are early in our development efforts, and we only have one product candidate in a clinical trial. Our other product candidate is in IND-enabling studies. If we are unable to commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed.
- We may not be successful in our efforts to use our product engine to build a pipeline of product candidates.
- Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. The results of preclinical studies and early clinical trials may not be predictive of future results. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.
- Because we are developing some of our product candidates for the treatment of diseases in which there is little clinical experience and, in some cases, using new endpoints or methodologies, such as the measurement of DUX4-driven gene expression in muscle biopsies in our Phase 2b clinical trial of losmapimod for the treatment of FSHD, the FDA or other regulatory authorities may not consider the endpoints of our clinical trials to predict or provide clinically meaningful results.
- If serious adverse events or unacceptable side effects are identified during the development of our product candidates, we may need to abandon or limit our development of some of our product candidates.
- We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.
- We expect to rely on contract manufacturing organizations to manufacture our product candidates. If we are unable to enter into such arrangements as expected or if such organizations do not meet our supply requirements, development and/or commercialization of our product candidates may be delayed.
- We rely, and expect to continue to rely, on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, which may harm our business.

- If we are unable to obtain, maintain, enforce and protect patent protection for our technology and product candidates or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully develop and commercialize our technology and product candidates may be adversely affected. The composition of matter patents for losmapimod licensed from GSK are expected to expire in 2023. Although we have filed patent applications directed to new methods of using losmapimod and other p38 inhibitors to treat FSHD that, if granted, would be expected to expire in 2038, we cannot be certain that any patents will be granted in respect of these patent applications. We do not own or in-license any patented intellectual property related to our product engine.
- If we fail to comply with our obligations in our intellectual property licenses and funding arrangements with third parties, or otherwise experience disruptions to our business relationships with our licensors, we could lose intellectual property rights that are important to our business.

Our Corporate Information

We were incorporated under the laws of the state of Delaware on August 18, 2015 under the name Fulcrum Therapeutics, Inc. Our principal executive offices are located at 26 Landsdowne Street, Cambridge, Massachusetts 02139, and our telephone number is (617) 651-8851. Our website address is <http://www.fulcrumtx.com>. The information contained on, or that can be accessed through, our website is not a part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

Implications of Being an Emerging Growth Company

As a company with less than \$1.07 billion in revenue during our last fiscal year, we qualify as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and we may remain an emerging growth company for up to five years or until such earlier time as we have more than \$1.07 billion in annual revenue, the market value of our stock held by non-affiliates is more than \$700 million or we issue more than \$1 billion of non-convertible debt over a three-year period. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure and other requirements that are applicable to public companies that are not emerging growth companies. In particular, in this prospectus, we have provided only two years of audited financial statements and have not included all of the executive compensation related information that would be required if we were not an emerging growth company. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold stock.

THE OFFERING

Common stock offered	shares
Common stock to be outstanding immediately following this offering	shares
Option to purchase additional shares	We have granted the underwriters an option for a period of 30 days to purchase up to additional shares of our common stock.
Use of proceeds	<p>We estimate that the net proceeds from this offering will be approximately \$ million (or approximately \$ million if the underwriters exercise their option to purchase additional shares in full), based on an assumed initial public offering price of \$ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.</p> <p>We intend to use the net proceeds from this offering, together with our existing cash and cash equivalents, to advance losmapimod for FSHD, to advance our hemoglobinopathies program, to fund our ongoing product engine and discovery efforts and for working capital and other general corporate purposes. See "Use of Proceeds."</p>
Risk factors	You should read the "Risk Factors" section of this prospectus for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.
Proposed Nasdaq Global Market symbol	"FULC"

The number of shares of our common stock to be outstanding after this offering is based on 19,430,506 shares of our common stock outstanding as of April 30, 2019, including 6,972,076 shares of unvested restricted stock subject to repurchase by us, and 112,500,000 shares of our common stock issuable upon the automatic conversion of all outstanding shares of our preferred stock upon the closing of this offering.

The number of shares of our common stock to be outstanding after this offering excludes:

- 10,503,582 shares of common stock issuable upon exercise of stock options outstanding as of April 30, 2019 at a weighted average exercise price of \$1.09 per share, and an additional 658,000 shares of common stock issuable upon the exercise of stock options granted subsequent to April 30, 2019, at a weighted average exercise price of \$1.58 per share;
- 2,565,912 shares of common stock reserved for future issuance under our 2016 Stock Incentive Plan, as amended, or the 2016 Plan, as of April 30, 2019; and
- 14,120,000 and 1,765,000 additional shares of our common stock that will become available for future issuance under our 2019 Stock Incentive Plan, of which our board of directors has granted options to purchase an aggregate of 2,159,544 shares of common stock to certain of our employees and non-employee directors effective upon the commencement of trading of our common stock on the Nasdaq Stock Market, and our 2019 Employee Stock Purchase Plan, respectively, each of which will become effective immediately prior to the effectiveness of the registration statement of which

this prospectus is a part, as well as any automatic increases in the number of shares of common stock reserved for future issuance under these plans.

Unless otherwise indicated, all information in this prospectus assumes:

- no exercise of the outstanding options described above;
- no exercise by the underwriters of their option to purchase additional shares of our common stock;
- the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 112,500,000 shares of our common stock upon the closing of this offering; and
- the filing and effectiveness of our restated certificate of incorporation and the adoption of our amended and restated bylaws upon the closing of this offering.

SUMMARY CONSOLIDATED FINANCIAL DATA

You should read the following summary consolidated financial data together with our consolidated financial statements and the related notes appearing at the end of this prospectus and the "Selected Consolidated Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections of this prospectus. We have derived the consolidated statement of operations data for the years ended December 31, 2017 and 2018 from our annual consolidated financial statements appearing at the end of this prospectus. The consolidated statement of operations data for the three months ended March 31, 2018 and 2019 and the consolidated balance sheet data as of March 31, 2019 have been derived from our interim consolidated financial statements appearing at the end of this prospectus and have been prepared on the same basis as the annual consolidated financial statements. In the opinion of management, the interim data reflect all normal recurring adjustments necessary for the fair presentation of the financial information in those statements. Our historical results are not necessarily indicative of the results that may be expected in the future, and our results for any interim period are not necessarily indicative of the results that should be expected for any full year or any other period.

	Year Ended December 31,		Three Months Ended March 31,	
	2017	2018	2018	2019
(in thousands, except per share data)				
Consolidated Statement of Operations Data:				
Operating expenses:				
Research and development	\$ 18,494	\$ 25,184	\$ 5,573	\$ 34,629
General and administrative	4,499	8,314	1,737	2,598
Total operating expenses	<u>22,993</u>	<u>33,498</u>	<u>7,310</u>	<u>37,227</u>
Loss from operations	<u>(22,993)</u>	<u>(33,498)</u>	<u>(7,310)</u>	<u>(37,227)</u>
Other income, net:				
Interest income, net	1	518	—	377
Other income	28	392	370	7
Net loss and comprehensive loss	<u>\$ (22,964)</u>	<u>\$ (32,588)</u>	<u>\$ (6,940)</u>	<u>\$ (36,843)</u>
Cumulative convertible preferred stock dividends	<u>\$ (2,407)</u>	<u>\$ (6,559)</u>	<u>(828)</u>	<u>(3,041)</u>
Net loss attributable to common stockholders	<u>\$ (25,371)</u>	<u>\$ (39,147)</u>	<u>\$ (7,768)</u>	<u>\$ (39,884)</u>
Net loss per share attributable to common stockholders, basic and diluted ⁽¹⁾	<u>\$ (5.09)</u>	<u>\$ (4.45)</u>	<u>\$ (1.09)</u>	<u>\$ (3.47)</u>
Weighted average number of common shares used in net loss per share attributable to common stockholders, basic and diluted ⁽¹⁾	<u>4,980</u>	<u>8,799</u>	<u>7,134</u>	<u>11,497</u>
Pro forma net loss per share attributable to common stockholders, basic and diluted ⁽¹⁾		<u>\$ (0.43)</u>		<u>\$ (0.31)</u>
Pro forma weighted average number of common shares used in net loss per share attributable to common stockholders, basic and diluted ⁽¹⁾		<u>76,655</u>		<u>118,580</u>

- (1) See Note 12 to our annual and interim consolidated financial statements appearing at the end of this prospectus for details on the calculation of basic and diluted net loss per share attributable to common stockholders and basic and diluted pro forma net loss per share attributable to common stockholders.

	As of March 31, 2019	
	Actual	Pro Forma As Adjusted ⁽³⁾
Consolidated Balance Sheet Data:		
Cash and cash equivalents	\$ 62,452	\$ 62,452
Working capital ⁽¹⁾	59,306	59,306
Total assets	75,588	75,588
Convertible preferred stock	165,136	—
Total stockholders' (deficit) equity	(99,687)	65,449

- (1) We define working capital as current assets less current liabilities.
- (2) The pro forma balance sheet data give effect to the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 112,500,000 shares of common stock upon the closing of this offering.
- (3) The pro forma as adjusted balance sheet data give further effect to our issuance and sale of _____ shares of our common stock in this offering at an assumed initial public offering price of \$ _____ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The pro forma as adjusted information discussed above is illustrative only and will change based on the actual initial public offering price and other terms of this offering determined at pricing. A \$1.00 increase (decrease) in the assumed initial public offering price of \$ _____ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash and cash equivalents, working capital, total assets and total stockholders' equity by \$ _____ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. An increase (decrease) of 1,000,000 shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash and cash equivalents, working capital, total assets and total stockholders' equity by \$ _____ million, assuming no change in the assumed initial public offering price per share and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below together with all of the other information contained in this prospectus, including our consolidated financial statements and the related notes appearing at the end of this prospectus, before deciding to invest in our common stock. If any of the following risks actually occur, our business, prospects, operating results and financial condition could suffer materially. In such event, the trading price of our common stock could decline and you might lose all or part of your investment.

Risks Related to our Financial Position and Need for Additional Capital

We have incurred significant losses since our inception. We expect to incur losses over the next several years and may never achieve or maintain profitability.

Since inception, we have incurred significant operating losses. Our net loss was \$23.0 million for the year ended December 31, 2017, \$32.6 million for the year ended December 31, 2018 and \$36.8 million for the three months ended March 31, 2019. As of March 31, 2019, we had an accumulated deficit of \$105.0 million. To date, we have financed our operations primarily through the issuance of convertible notes and convertible preferred stock. We have devoted substantially all of our financial resources and efforts to research and development, including clinical trials and preclinical studies. We are still in the early stages of development of our product candidates, and we have not completed development of any product candidates. We expect to continue to incur significant expenses and operating losses over the next several years. Our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially as we:

- continue our clinical development of losmapimod, including our ongoing Phase 1 clinical trial and planned Phase 2b clinical trial and Phase 2 open label clinical trial;
- continue investigational new drug application, or IND, enabling studies and prepare for a planned Phase 1 clinical trial of FTX-HbF;
- advance clinical-stage product candidates into later stage trials;
- pursue the discovery of drug targets for other rare diseases and the subsequent development of any resulting product candidates;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- scale up our manufacturing processes and capabilities, or arrange for a third party to do so on our behalf, to support our clinical trials of our product candidates and commercialization of any of our product candidates for which we may obtain marketing approval;
- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain regulatory approval;
- acquire or in-license products, product candidates, technologies and/or data referencing rights;
- make any milestone payments to affiliates of GlaxoSmithKline plc, or GSK, under our right of reference and license agreement with GSK upon the achievement of specified clinical or regulatory milestones;
- maintain, expand, enforce, defend and protect our intellectual property;
- hire additional clinical, quality control and scientific personnel; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts and our operations as a public company.

To become and remain profitable, we must succeed in developing, and eventually commercializing, a product or products that generate significant revenue. The ability to achieve this success will require us to be effective in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, discovering additional product candidates, obtaining regulatory approval for these product candidates and manufacturing, marketing and selling any products for which we may obtain regulatory approval. We are only in the preliminary stages of most of these activities. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability. Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. Our expenses will increase if, among other things:

- we are required by the U.S. Food and Drug Administration, or the FDA, the European Medicines Agency, or the EMA, or other regulatory authorities to perform trials or studies in addition to, or different than, those expected;
- there are any delays in completing our clinical trials or the development of any of our product candidates; or
- there are any third-party challenges to our intellectual property or we need to defend against any intellectual property-related claim.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our pipeline of product candidates or even continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

We will need substantial additional funding. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

We expect to devote substantial financial resources to our ongoing and planned activities, particularly as we continue our Phase 1 clinical trial of losmapimod and prepare for a planned Phase 2b clinical trial and Phase 2 open label clinical trial of losmapimod and planned Phase 1 clinical trial of FTX-HbF; and continue research and development and initiate additional clinical trials of, and seek regulatory approval for, these and other product candidates. We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we advance our preclinical activities and clinical trials. In addition, if we obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution. Furthermore, upon the closing of this offering, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on acceptable terms, we could be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

Our future capital requirements will depend on many factors, including:

- the progress, costs and results of our ongoing Phase 1 clinical trial of losmapimod;
- the scope, progress, results and costs of discovery research, preclinical development, laboratory testing and clinical trials for our product candidates, including our planned Phase 2b clinical trial and planned Phase 2 open label clinical trial of losmapimod and our planned Phase 1 clinical trial of FTX-HbF;
- the number of and development requirements for other product candidates that we pursue;
- the costs, timing and outcome of regulatory review of our product candidates;

- our ability to enter into contract manufacturing arrangements for supply of active pharmaceutical ingredient, or API, and manufacture of our product candidates and the terms of such arrangements;
- our ability to establish and maintain strategic collaborations, licensing or other arrangements and the financial terms of such arrangements;
- the payment or receipt of milestones and receipt of other collaboration-based revenues, if any;
- the costs and timing of future commercialization activities, including product manufacturing, sales, marketing and distribution, for any of our product candidates for which we may receive marketing approval;
- the amount and timing of revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property and proprietary rights and defending any intellectual property-related claims; and
- the extent to which we acquire or in-license other products, product candidates, technologies or data referencing rights.

As of March 31, 2019, we had cash and cash equivalents of approximately \$62.5 million. We believe that the net proceeds from this offering, together with our existing cash and cash equivalents as of March 31, 2019, will enable us to fund our operating expenses and capital expenditure requirements through . However, we have based this estimate on assumptions that may prove to be wrong, and our operating plan may change as a result of many factors currently unknown to us. As a result, we could deplete our capital resources sooner than we currently expect.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Commercial revenues, if any, will not be derived unless and until we can achieve sales of products, which we do not anticipate for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. If adequate funds are not available to us on a timely basis, we may be required to delay, limit, reduce or terminate preclinical studies, clinical trials or other development activities for one or more of our product candidates or discovery stage programs or delay, limit, reduce or terminate our establishment of sales and marketing capabilities or other activities that may be necessary to commercialize our product candidates.

Raising additional capital may cause dilution to our stockholders, including purchasers of our common stock in this offering, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, selling or licensing our assets, making capital expenditures or declaring dividends.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We commenced activities in 2015 and are an early-stage company. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, developing our technology, identifying drug targets and potential product candidates, undertaking preclinical studies and conducting one early-stage clinical trial. We have not yet demonstrated our ability to successfully develop any product candidate, obtain regulatory approvals, manufacture a commercial scale product or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing products.

In addition, as our business grows, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to transition at some point from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We expect our financial condition and operating results to fluctuate significantly from quarter-to-quarter and year-to-year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern.

We may be forced to delay or reduce the scope of our development programs and/or limit or cease our operations if we are unable to obtain additional funding to support our current operating plan. We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern. As of March 31, 2019, we had approximately \$62.5 million in cash and cash equivalents. Based on our available cash resources, we believe we do not have sufficient cash on hand to support current operations for at least one year from the date that the consolidated financial statements for the year ended December 31, 2018 and the consolidated financial statements for the three months ended March 31, 2019 appearing at the end of this prospectus were issued. This condition raises substantial doubt about our ability to continue as a going concern for at least one year from the date of issuance of the financial statements appearing at the end of this prospectus, and our independent registered public accounting firm's report on our consolidated financial statements appearing at the end of this prospectus includes a going concern uncertainty paragraph. We will need to raise additional capital in this offering and/or otherwise to fund our future operations and remain as a going concern. However, we cannot guarantee that we will be able to obtain sufficient additional funding in this offering or otherwise or that such funding, if available, will be obtainable on terms satisfactory to us. In the event that we are unable to obtain sufficient additional funding, there can be no assurance that we will be able to continue as a going concern.

Comprehensive tax reform legislation passed in 2017 could adversely affect our business and financial condition.

On December 22, 2017, the U.S. government enacted legislation commonly referred to as the Tax Cuts and Jobs Act, or the TCJA, which significantly reformed the Internal Revenue Code of 1986, as amended, or the Code. The TCJA, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for net interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses, or NOLs, to 80% of current year taxable income and elimination of NOL carrybacks, in each case, for losses arising in taxable years beginning after December 31, 2017 (though any such NOLs may be carried forward indefinitely), one-time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the TCJA remains uncertain and our business and financial condition could be adversely affected. In addition, how various states will respond to the TCJA continues to be uncertain. The impact of this tax reform on holders of our common stock is also uncertain and could be adverse. We urge prospective investors in our common stock to consult with their legal and tax advisors with respect to TCJA and the potential tax consequences of investing in or holding our common stock.

Our ability to use our NOLs and research and development tax credit carryforwards to offset future taxable income may be subject to certain limitations.

As of December 31, 2018, we had federal and state net operating loss carryforwards of \$60.7 million and \$60.5 million, respectively, which begin to expire in 2035. Approximately \$29.7 million of the federal net operating losses can be carried forward indefinitely. As of December 31, 2018, we also had federal and state research and development tax credit carryforwards of \$1.5 million and \$1.3 million, respectively, which begin to expire in 2035. These net operating loss and tax credit carryforwards could expire unused and be unavailable to offset future income tax liabilities.

We have a history of cumulative losses and anticipate that we will continue to incur significant losses in the foreseeable future; thus, we do not know whether or when we will generate taxable income necessary to utilize our NOLs or research and development tax credit carryforwards.

In general, under Section 382 of the Code and corresponding provisions of state law, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change NOLs and research and development tax credit carryforwards to offset future taxable income. We have not conducted a study to assess whether any such ownership changes have occurred. We may have experienced such ownership changes in the past and may experience such ownership changes in the future as a result of this offering and/or subsequent changes in our stock ownership (which may be outside our control). As a result, if, and to the extent that, we earn net taxable income, our ability to use our pre-change NOLs and research and development tax credit carryforwards to offset such taxable income may be subject to limitations. Our NOLs or credits may also be impaired under state law.

In addition, as described above in "Comprehensive tax reform legislation passed in 2017 could adversely affect our business and financial condition," the TCJA includes changes to U.S. federal tax rates and the rules governing NOL carryforwards that may significantly impact our ability to utilize our NOLs to offset taxable income in the future.

Risks Related to the Discovery and Development of our Product Candidates

We are early in our development efforts, and we only have one product candidate in a clinical trial. Our other product candidate is in IND-enabling studies. If we are unable to commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed.

We are early in our development efforts, and we have advanced only one candidate into clinical trials, losmapimod for the treatment of facioscapulohumeral muscular dystrophy, or FSHD. FTX-HbF, our other product candidate, is in IND-enabling studies. We have invested substantially all of our efforts and financial resources in our proprietary product engine to identify and validate cellular drug targets that can potentially modulate gene expression to address the root cause of rare diseases. Our ability to generate product revenues, which we do not expect will occur for many years, if ever, will depend heavily on the successful development, regulatory approval and eventual commercialization of our product candidates. The success of our product candidates will depend on several factors, including the following:

- successfully completing preclinical studies and clinical trials;
- acceptance by the FDA or other regulatory agencies of the INDs, clinical trial applications, or CTAs, or other regulatory filings for losmapimod, FTX-HbF and future product candidates;
- expanding and maintaining a workforce of experienced scientists and others to continue to develop our product candidates;
- successfully applying for and receiving marketing approvals from applicable regulatory authorities;
- obtaining and maintaining intellectual property protection and regulatory exclusivity for our product candidates;
- making arrangements with third-party manufacturers for, or establishing, commercial manufacturing capabilities;
- establishing sales, marketing and distribution capabilities and successfully launching commercial sales of the products, if and when approved, whether alone or in collaboration with others;
- acceptance of the products, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- obtaining and maintaining coverage, adequate pricing and adequate reimbursement from third-party payors, including government payors;
- maintaining, enforcing, defending and protecting our rights in our intellectual property portfolio;
- not infringing, misappropriating or otherwise violating others' intellectual property or proprietary rights; and
- maintaining a continued acceptable safety profile of the products following receipt of any regulatory approvals.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully develop and commercialize our product candidates, which would materially harm our business.

We may not be successful in our efforts to use our product engine to build a pipeline of product candidates.

A key element of our strategy is to use our proprietary product engine to identify and validate cellular drug targets that can potentially modulate gene expression to address the root cause of rare diseases, with an initial focus on identifying small molecules specific to the identified cellular target. Even if we are

successful in identifying drug targets and potential product candidates, such candidates that we identify may not be suitable for clinical development, including as a result of being shown to have harmful side effects or other characteristics that indicate that they are unlikely to receive marketing approval and achieve market acceptance. Identifying, developing, obtaining regulatory approval for and commercializing additional product candidates will require substantial additional funding and is prone to the risks of failure inherent in product development. We cannot provide you any assurance that we will be able to successfully identify additional product candidates with our product engine, advance any of these additional product candidates through the development process or successfully commercialize any such additional product candidates. Regulatory authorities have substantial discretion in the approval process and may cause delays in the approval or rejection of an application. As a result of these factors, it is difficult for us to predict the time and cost of product candidate development. There can be no assurance that any development problems we experience in the future related to our proprietary product engine or any of our research or development programs will not cause significant delays or unanticipated costs, or that such development problems can be solved. If we do not successfully identify, develop, obtain regulatory approval for and commercialize product candidates based upon our technological approach, we will not be able to generate product revenues.

Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. The results of preclinical studies and early clinical trials may not be predictive of future results. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

We have one product candidate in clinical development and one product candidate in IND-enabling studies. The risk of failure for each of our product candidates is high. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. We have not yet begun or completed a pivotal clinical trial of any product candidate. Clinical trials may fail to demonstrate that our product candidates are safe for humans and effective for indicated uses. Even if the clinical trials are successful, changes in marketing approval policies during the development period, changes in or the enactment or promulgation of additional statutes, regulations or guidance or changes in regulatory review for each submitted product application may cause delays in the approval or rejection of an application.

Before we can commence clinical trials for a product candidate, we must complete extensive preclinical testing and studies that support our planned INDs and other regulatory filings in the United States and abroad. We cannot be certain of the timely completion or outcome of our preclinical testing and studies and cannot predict if the FDA or other regulatory agencies will accept our proposed clinical programs or if the outcome of our preclinical testing and studies will ultimately support the further development of our current or future product candidates. As a result, we cannot be sure that we will be able to submit INDs or similar applications for our preclinical programs on the timelines we expect, if at all, and we cannot be sure that submission of INDs or similar applications will result in the FDA or other regulatory authorities allowing clinical trials to begin. Furthermore, product candidates are subject to continued preclinical safety studies, which may be conducted concurrent with our clinical testing. The outcomes of these safety studies may delay the launch of or enrollment in future clinical trials and could impact our ability to continue to conduct our clinical trials.

Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, or at all. A failure of one or more clinical trials can occur at any stage of testing, which may result from a multitude of factors, including, but not limited to, flaws in study design, dose selection issues, placebo effects, patient enrollment criteria and failure to demonstrate favorable safety or

efficacy traits. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and preliminary or interim results of a clinical trial do not necessarily predict final results. For example, our product candidates may fail to show the desired safety and efficacy in clinical development despite positive results in preclinical studies or having successfully advanced through initial clinical trials. Losmapimod may not be effective at reducing DUX4-driven gene expression or, even if losmapimod successfully reduces expression of DUX4-driven genes, such reduction may not result in overall clinical benefit. A lack of clinical benefit may be due to insufficient dosing or for other reasons. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in preclinical testing and earlier-stage clinical trials, and we cannot be certain that we will not face similar setbacks. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. Furthermore, the failure of any of our product candidates to demonstrate safety and efficacy in any clinical trial could negatively impact the perception of our other product candidates and/or cause the FDA or other regulatory authorities to require additional testing before approving any of our product candidates.

In February 2019, we entered into a right of reference and license agreement, or the GSK Agreement, with affiliates of GSK pursuant to which, among other things, GSK granted us a right of reference to certain INDs filed with the FDA and controlled by GSK or its affiliates relating to losmapimod and an exclusive worldwide license to certain of GSK's preclinical and clinical data with respect to losmapimod. Although losmapimod was originally evaluated by GSK in nearly 3,500 subjects, GSK did not evaluate losmapimod in FSHD or in any other muscular dystrophy, and most of the subjects in these trials were given a dose that was lower than our planned dosage of 15 mg of losmapimod twice per day, so the safety data generated from GSK's clinical trials of losmapimod may not be predictive or indicative of the results of our clinical trials. Similarly, while we believe the safety data from GSK's clinical trials may, in part, enable us to apply for accelerated approval, there can be no assurance that this will happen. Regulatory authorities may also raise questions regarding the transition in the future from GSK-manufactured tablets to tablets manufactured by us or another party, and we may be required to conduct comparability assessments, which could result in delays in development and additional costs.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- regulators or institutional review boards, or IRBs, may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- regulators may decide the design of our clinical trials is flawed, for example if our trial protocol does not evaluate treatment effects in trial subjects for a sufficient length of time;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- we may be unable to establish clinical endpoints that applicable regulatory authorities would consider clinically meaningful, or, if we seek accelerated approval, biomarker efficacy endpoints that applicable regulatory authorities would consider likely to predict clinical benefit;
- preclinical testing may produce results based on which we may decide, or regulators may require us, to conduct additional preclinical studies before we proceed with certain clinical trials, limit the scope of our clinical trials, halt ongoing clinical trials or abandon product development programs;

- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we may decide, or regulators or IRBs may require us, to suspend or terminate clinical trials of our product candidates for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- regulators or IRBs may require us to perform additional or unanticipated clinical trials to obtain approval or we may be subject to additional post-marketing testing requirements to maintain regulatory approval;
- regulators may revise the requirements for approving our product candidates, or such requirements may not be as we anticipate;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate;
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or IRBs to suspend or terminate the trials; and
- regulators may withdraw their approval of a product or impose restrictions on its distribution, such as in the form of a risk evaluation and mitigation strategy, or REMS.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling or a REMS that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

Our product development costs will also increase if we experience delays in testing or in obtaining marketing approvals. We do not know whether any of our preclinical studies or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. We may also determine to change the design or protocol of one or more of our clinical trials, including to add additional patients or arms, which could result in increased costs and expenses and/or delays. Significant preclinical study or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

Because we are developing some of our product candidates for the treatment of diseases in which there is little clinical experience and, in some cases, using new endpoints or methodologies, the FDA or other regulatory authorities may not consider the endpoints of our clinical trials to predict or provide clinically meaningful results.

There are currently no therapies approved to treat FSHD, and there may be no therapies approved to treat the underlying causes of diseases that we attempt to address or may address in the future. As a result, the design and conduct of clinical trials of product candidates for the treatment of these diseases may take longer, be more costly or be less effective as part of the novelty of development in these diseases. In some cases, we may use new or novel endpoints or methodologies, such as the optimized time up and go test we intend to use in our losmapimod clinical trials, which we refer to as the FSHD-TUG test, and the FDA or other regulatory authorities may not consider the endpoints of our clinical trials to provide clinically meaningful results. Even if applicable regulatory authorities do not object to our proposed endpoints in an earlier stage clinical trial, such regulatory authorities may require evaluation of additional or different clinical endpoints in later-stage clinical trials. Additionally, if we pursue accelerated approval for certain product candidates, the FDA or another regulatory authority may determine that the biomarker efficacy endpoint we select for evaluation is not sufficiently predictive of clinical benefit to support accelerated approval. For example, if we pursue accelerated approval with the FDA for losmapimod for the treatment of FSHD, the FDA may determine that our proposed biomarker efficacy endpoint of measuring DUX4-driven gene expression as a biomarker in muscle biopsies is inadequate to accurately capture treatment effects in muscle over time or is not sufficiently predictive of clinical benefit to support accelerated approval. The FDA may also determine that the measurement interval for our Phase 2b clinical trial is too short to evaluate the potential clinical benefit of losmapimod for FSHD where the progression of symptoms is relatively slow and chronic dosing is required.

Even if the FDA does find our clinical trial success criteria to be sufficiently validated and clinically meaningful, we may not achieve the pre-specified endpoint to a degree of statistical significance in any pivotal or other clinical trials we may conduct for our product candidates. Further, even if we do achieve the pre-specified criteria, our trials may produce results that are unpredictable or inconsistent with the results of the more traditional efficacy endpoints in the trial. The FDA also could give overriding weight to other efficacy endpoints over a primary endpoint, even if we achieve statistically significant results on that primary endpoint, if we do not do so on our secondary efficacy endpoints. The FDA also weighs the benefits of a product against its risks and the FDA may view the efficacy results in the context of safety as not being supportive of approval. Other regulatory authorities in Europe and other countries may make similar findings with respect to these endpoints.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

Identifying and qualifying patients to participate in clinical trials for our product candidates is critical to our success. Successful and timely completion of clinical trials will require that we enroll a sufficient number of patients who remain in the trial until its conclusion. We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside of the United States. Because of our primary focus on rare diseases, we may have difficulty enrolling a sufficient number of eligible patients.

Patient enrollment is affected by a variety of other factors, including:

- the prevalence and severity of the disease under investigation;
- the eligibility criteria for the trial in question;
- the perceived risks and benefits of the product candidate under trial;
- the requirements of the trial protocols, including invasive procedures such as muscle biopsies;

- the availability of existing treatments for the indications for which we are conducting clinical trials;
- the ability to recruit clinical trial investigators with the appropriate competencies and experience;
- the efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;
- the proximity and availability of clinical trial sites for prospective patients;
- the conduct of clinical trials by competitors for product candidates that treat the same indications as our product candidates;
- the ability to identify specific patient populations for biomarker-defined trial cohort(s); and
- the cost to, or lack of adequate compensation for, prospective patients.

Our inability to locate and enroll a sufficient number of patients for our clinical trials would result in significant delays, could require us to abandon one or more clinical trials altogether and could delay or prevent our receipt of necessary regulatory approvals. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

If serious adverse events or unacceptable side effects are identified during the development of our product candidates, we may need to abandon or limit our development of some of our product candidates.

If our product candidates are associated with serious adverse events or undesirable side effects in clinical trials or have characteristics that are unexpected in clinical trials or preclinical testing, we may need to abandon their development or limit development to more narrow uses or subpopulations in which the serious adverse events, undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. In pharmaceutical development, many compounds that initially show promise in early-stage or clinical testing are later found to cause side effects that delay or prevent further development of the compound.

Additionally, if results of our clinical trials reveal unacceptable side effects, we, the FDA or the IRBs at the institutions in which our studies are conducted could suspend or terminate our clinical trials or the FDA or comparable foreign regulatory authorities could order us to cease clinical trials or deny approval of our product candidates for any or all targeted indications. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete any of our clinical trials. If we elect or are forced to suspend or terminate any clinical trial of our product candidates, the commercial prospects of such product candidate will be harmed, and our ability to generate product revenue from such product candidate will be delayed or eliminated. Any of these occurrences could materially harm our business.

If any of our product candidates receives marketing approval and we, or others, later discover that the drug is less effective than previously believed or causes undesirable side effects that were not previously identified, our ability to market the drug could be compromised.

Clinical trials of our product candidates are conducted in carefully defined subsets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. If one or more of our product candidates receives regulatory approval, and we, or others, later discover that they are less effective than previously believed,

or cause undesirable side effects, a number of potentially significant negative consequences could result, including:

- withdrawal or limitation by regulatory authorities of approvals of such product;
- seizure of the product by regulatory authorities;
- recall of the product;
- restrictions on the marketing of the product or the manufacturing process for any component thereof;
- requirement by regulatory authorities of additional warnings on the label, such as a "black box" warning or contraindication;
- requirement that we implement a REMS or create a medication guide outlining the risks of such side effects for distribution to patients;
- commitment to expensive post-marketing studies as a prerequisite of approval by regulatory authorities of such product;
- the product may become less competitive;
- initiation of regulatory investigations and government enforcement actions;
- initiation of legal action against us to hold us liable for harm caused to patients; and
- harm to our reputation and resulting harm to physician or patient acceptance of our products.

Any of these events could prevent us from achieving or maintaining market acceptance of a particular product candidate, if approved, and could significantly harm our business, financial condition, and results of operations.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we are focusing our research and development efforts on rare neuromuscular disorders, hemoglobinopathies and central nervous system diseases. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. Failure to allocate resources or capitalize on strategies in a successful manner will have an adverse impact on our business.

We are conducting a Phase 1 clinical trial of losmapimod in patients with FSHD in Europe and currently plan to conduct additional clinical trials for our product candidates at sites outside the United States, and the FDA may not accept data from trials conducted in such locations.

We are currently conducting a Phase 1 clinical trial of losmapimod in patients with FSHD in Europe, and we plan to conduct additional clinical trials outside the United States. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of these data is subject to conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted and be performed by qualified investigators in accordance with ethical principles. The trial population must

also adequately represent the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will depend on its determination that the trials also complied with all applicable U.S. laws and regulations. If the FDA does not accept the data from any trial that we conduct outside the United States, it would likely result in the need for additional trials, which would be costly and time-consuming and could delay or permanently halt our development of the applicable product candidates.

Risks Related to the Commercialization of our Product Candidates

Even if any of our product candidates receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success, and the market opportunity for any of our product candidates, if approved, may be smaller than we estimate.

If any of our product candidates receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. Efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may not be successful. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and potential advantages of our product candidates compared to the advantages and relative risks of alternative treatments;
- the effectiveness of sales and marketing efforts;
- the cost of treatment in relation to alternative treatments, including any similar generic treatments;
- our ability to offer our products, if approved, for sale at competitive prices;
- the clinical indications for which the product is approved;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- the timing of market introduction of competitive products;
- the availability of third-party coverage and adequate reimbursement, and patients' willingness to pay out of pocket for required co-payments or in the absence of third-party coverage or adequate reimbursement;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our products, if approved, together with other medications.

Our assessment of the potential market opportunity for our product candidates is based on industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties, one of which we commissioned. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. While we believe these industry publications and third-party research, surveys and studies are reliable, we have not independently verified such data. We commissioned Clarion Healthcare, LLC to conduct market research

with physicians and payors to better understand the commercial landscape and to assist in our commercial planning. A total of 14 physicians in the United States, the European Union and Asia and nine payors and payor experts in the United States and the European Union were surveyed. As the survey involved a limited number of physicians and payors, the results from such survey may be less reflective of market opportunity than a survey conducted with a larger sample size. Our estimates of the potential market opportunities for our product candidates include several key assumptions based on our industry knowledge, industry publications and third-party research, surveys and studies, which may be based on a small sample size and fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions. If any of our assumptions or estimates, or these publications, research, surveys or studies prove to be inaccurate, then the actual market for any of our product candidates may be smaller than we expect, and as a result our product revenue may be limited and it may be more difficult for us to achieve or maintain profitability.

If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution agreements with third parties, we may not be successful in commercializing our product candidates if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any product for which we have obtained marketing approval, we will need to establish a sales, marketing and distribution organization, either ourselves or through collaborations or other arrangements with third parties.

In the future, we expect to build a focused, specialty sales and marketing infrastructure to market some of our product candidates in the United States, if and when they are approved. There are risks involved with establishing our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force is expensive and time-consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. These efforts may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales, marketing, coverage or reimbursement, customer service, medical affairs and other support personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future products;
- the inability of reimbursement professionals to negotiate arrangements for formulary access, reimbursement and other acceptance by payors;
- the inability to price our products at a sufficient price point to ensure an adequate and attractive level of profitability;
- restricted or closed distribution channels that make it difficult to distribute our products to segments of the patient population;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we are unable to establish our own sales, marketing and distribution capabilities and we enter into arrangements with third parties to perform these services, our product revenues and our profitability, if

any, are likely to be lower than if we were to market, sell and distribute any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute our product candidates or may be unable to do so on terms that are acceptable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The development and commercialization of new drug products is highly competitive. We face competition with respect to our current product candidates, and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of many of the disease indications for which we are developing our product candidates. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

For example, we are aware of several product candidates in clinical development that could be competitive with product candidates that we may successfully develop and commercialize. Acceleron Pharma, Inc., or Acceleron, has a product candidate currently in Phase 2a clinical development for FSHD. Novartis AG, Global Blood Therapeutics, Inc., GlycoMimetics Inc., Pfizer, Inc., bluebird bio, Inc., Aruvant Sciences, Inc., EpiDestiny, Inc., or EpiDestiny (in collaboration with Novo Nordisk A/S), Imara, Inc. and Sangamo Therapeutics Inc., or Sangamo (in collaboration with Bioverativ Inc.), are developing therapeutic approaches for patients with sickle cell disease, or SCD. Acceleron (in collaboration with Celgene Corp.), Bellicum Pharmaceuticals, Inc., Kiadis Pharma, EpiDestiny (in collaboration with Novo Nordisk A/S), Orchard Therapeutics plc, Sangamo (in collaboration with Bioverativ, Inc.) and CRISPR Therapeutics AG (in collaboration with Vertex Pharmaceuticals, Inc.) are developing therapeutic approaches for patients with b-thalassemia.

See "Business—Competition" for additional information regarding competing products and product candidates.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products. If our product candidates achieve marketing approval, we expect that they will be priced at a significant premium over competitive generic products.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do.

Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

If the market opportunities for our product candidates are smaller than we believe they are, our revenue may be adversely affected, and our business may suffer. Because the target patient populations of our product candidates are small, and the addressable patient population even smaller, we must be able to successfully identify patients and capture a significant market share to achieve profitability and growth.

We focus our research and product development on treatments for rare diseases. Given the small number of patients who have the diseases that we are targeting, it is critical to our ability to grow and become profitable that we continue to successfully identify patients with these rare diseases. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including the scientific literature, surveys of clinics, patient foundations or market research that we conducted, and may prove to be incorrect or contain errors. New studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. The effort to identify patients with diseases we seek to treat is in early stages, and we cannot accurately predict the number of patients for whom treatment might be possible. Additionally, the potentially addressable patient population for each of our product candidates may be limited or may not be amenable to treatment with our product candidates, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business. Further, even if we obtain significant market share for our product candidates, because the potential target populations are very small, we may never achieve profitability despite obtaining such significant market share.

Our target patient populations are relatively small, and there is currently no standard of care treatment directed at some of our target indications, such as FSHD. As a result, the pricing and reimbursement of our product candidates, if approved, is uncertain, but must be adequate to support commercial infrastructure. If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell our product candidates will be adversely affected.

We expect to rely on contract manufacturing organizations to manufacture our product candidates. If we are unable to enter into such arrangements as expected or if such organizations do not meet our supply requirements, development and/or commercialization of our product candidates may be delayed.

We expect to rely on third parties to manufacture clinical supplies of our product candidates and commercial supplies of our products, if and when approved for marketing by applicable regulatory authorities, as well as for packaging, sterilization, storage, distribution and other production logistics. If we are unable to enter into such arrangements on the terms or timeline we expect, development and/or commercialization of our product candidates may be delayed. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or manufacture our product candidates in accordance with regulatory requirements, if there are disagreements between us and such parties or if such parties are unable to expand capacities to support commercialization of any of our product candidates for which we obtain marketing approval, we may not be able to fulfill, or may be delayed in producing sufficient product candidates to meet, our supply requirements. These facilities may also be affected by natural disasters, such as floods or fire, or such facilities could face manufacturing issues, such as contamination or regulatory concerns following a regulatory inspection of such facility. In such instances, we may need to locate an appropriate replacement third-party facility and establish a contractual

relationship, which may not be readily available or on acceptable terms, which would cause additional delay and increased expense, including as a result of additional required FDA approvals, and may have a material adverse effect on our business.

Our third-party manufacturers will be subject to inspection and approval by the FDA before we can commence the manufacture and sale of any of our product candidates, and thereafter subject to FDA inspection from time to time. Failure by our third-party manufacturers to pass such inspections and otherwise satisfactorily complete the FDA approval regimen with respect to our product candidates may result in regulatory actions such as the issuance of FDA Form 483 notices of observations, warning letters or injunctions or the loss of operating licenses.

We or our third-party manufacturers may also encounter shortages in the raw materials or API necessary to produce our product candidates in the quantities needed for our clinical trials or, if our product candidates are approved, in sufficient quantities for commercialization or to meet an increase in demand, as a result of capacity constraints or delays or disruptions in the market for the raw materials or API, including shortages caused by the purchase of such raw materials or API by our competitors or others. The failure of us or our third-party manufacturers to obtain the raw materials or API necessary to manufacture sufficient quantities of our product candidates, may have a material adverse effect on our business.

Even if we are able to commercialize any product candidates, the products may become subject to unfavorable pricing regulations, third-party coverage or reimbursement practices or healthcare reform initiatives, which could harm our business.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

Our ability to commercialize any product candidates successfully also will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Coverage and reimbursement may not be available for any product that we commercialize and, even if these are available, the level of reimbursement may not be satisfactory. Reimbursement may affect the demand for, or the price of, any product candidate for which we obtain marketing approval. Obtaining and maintaining adequate reimbursement for our products may be difficult. We may be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies. If coverage and adequate reimbursement are not available or reimbursement is

available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or similar regulatory authorities outside of the United States. Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution expenses. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

There can be no assurance that our product candidates, even if they are approved for sale in the United States or in other countries, will be considered medically reasonable and necessary for a specific indication or cost-effective by third-party payors, or that coverage and an adequate level of reimbursement will be available or that third-party payors' reimbursement policies will not adversely affect our ability to sell our product candidates profitably.

Our future growth depends, in part, on our ability to penetrate foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties that, if they materialize, could harm our business.

Our future profitability will depend, in part, on our ability to commercialize our product candidates in markets outside of the United States and the European Union. If we commercialize our product candidates in foreign markets, we will be subject to additional risks and uncertainties, including:

- economic weakness, including inflation, or political instability in particular economies and markets;
- the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements, many of which vary between countries;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- tariffs and trade barriers, as well as other governmental controls and trade restrictions;
- other trade protection measures, import or export licensing requirements or other restrictive actions by U.S. or foreign governments;
- longer accounts receivable collection times;
- longer lead times for shipping;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- workforce uncertainty in countries where labor unrest is common;
- language barriers for technical training;
- reduced protection of intellectual property rights in some foreign countries, and related prevalence of generic alternatives to therapeutics;

- foreign currency exchange rate fluctuations and currency controls;
- differing foreign reimbursement landscapes;
- uncertain and potentially inadequate reimbursement of our products; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

If risks related to any of these uncertainties materializes, it could have a material adverse effect on our business.

Clinical trial and product liability lawsuits against us could divert our resources and could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We face an inherent risk of clinical trial and product liability exposure related to the testing of our product candidates in human clinical trials, and we will face an even greater risk if we commercially sell any products that we may develop. While we currently have no products that have been approved for commercial sale, the current and future use of product candidates by us in clinical trials, and the sale of any approved products in the future, may expose us to liability claims. These claims might be made by patients that use the product, healthcare providers, pharmaceutical companies or others selling such products. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend any related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any products that we may develop.

We currently hold \$10 million in clinical trial liability insurance coverage in the aggregate, with a per incident limit of \$10 million, which may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of our product candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. If a successful clinical trial or product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business operations could be impaired.

Risks Related to our Dependence on Third Parties

We rely, and expect to continue to rely, on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, which may harm our business.

We currently rely on third-party clinical research organizations to conduct our ongoing Phase 1 clinical trial of losmapimod and plan to rely on third-party clinical research organizations or third-party research collaboratives to conduct our planned clinical trials. We do not plan to independently conduct clinical trials

of our other product candidates. We expect to continue to rely on third parties, such as clinical research organizations, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials. These agreements might terminate for a variety of reasons, including a failure to perform by the third parties. If we need to enter into alternative arrangements, our product development activities might be delayed.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as good clinical practices, or GCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully develop and commercialize our product candidates. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors.

We also expect to rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential product revenue.

We plan to contract with third parties for the manufacture of our product candidates for preclinical and clinical testing and expect to continue to do so for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

We do not have any manufacturing facilities. Although we believe we have obtained sufficient losmapimod tablets from GSK to complete our planned Phase 2 clinical trials and that we have received a sufficient quantity of losmapimod API to complete further clinical trials in FSHD, we cannot be sure we have correctly estimated our drug product and API requirements or that such drug product or API will not expire before we want to use it. We intend to identify and engage a contract manufacturing organization to prepare our own API and to manufacture losmapimod tablets, but we may not be successful in entering into such arrangement or may be unable to do so on terms that are acceptable to us. Even if we have sufficient API to complete further clinical trials in FSHD, we would need to contract with a third-party manufacturer to convert the API into losmapimod tablets. While we believe that we have all the necessary information from GSK to enable any required technology transfer to a contract manufacturing organization, there can be no assurances that we will be able to effect such transfer in a timely manner.

We expect to rely on third parties for the manufacture of FTX-HbF and any future product candidates for preclinical and clinical testing, as well as for commercial manufacture if any of our product candidates receive marketing approval. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

We also expect to rely on third-party manufacturers or third-party collaborators for the manufacture of commercial supply of any other product candidates for which we or our collaborators obtain marketing approval. We may be unable to establish any agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

Third-party manufacturers may not be able to comply with current good manufacturing practices, or cGMP, regulations or similar regulatory requirements outside of the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products.

Our product candidates and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply or a source for bulk drug substance. If any of our future contract manufacturers cannot perform as agreed, we may be required to replace such manufacturers. Although we believe that there are several potential alternative manufacturers who could manufacture our product candidates, we may incur added costs and delays in identifying and qualifying any such replacement.

Our current and anticipated future dependence upon others for the manufacture of our product candidates or products may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

We may enter into collaborations with third parties for the development or commercialization of our product candidates. If our collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates and our business could be adversely affected.

While we have retained all rights to and are developing on our own our current product candidates, we may in the future enter into development, distribution or marketing arrangements with third parties with respect to our existing or future product candidates. Our likely collaborators for any sales, marketing, distribution, development, licensing or broader collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. We are not currently party to any such arrangement. However, if we do enter into any such arrangements with any third parties in the future, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities and efforts to successfully perform the functions assigned to them in these arrangements.

Collaborations that we enter into may not be successful, and any success will depend heavily on the efforts and activities of such collaborators. Collaborations pose a number of risks, including the following:

- collaborators have significant discretion in determining the amount and timing of efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development of our product candidates or may elect not to continue or renew development programs based on results of clinical trials or other studies, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may not pursue commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew commercialization programs based on results of clinical trials or other studies, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that may divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- we may not have access to, or may be restricted from disclosing, certain information regarding product candidates being developed or commercialized under a collaboration and, consequently, may have limited ability to inform our stockholders about the status of such product candidates on a discretionary basis;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates and products if the collaborators believe that the competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator may fail to comply with applicable regulatory requirements regarding the development, manufacture, distribution or marketing of a product candidate or product;
- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over intellectual property or proprietary rights, contract interpretation or the preferred course of development, might cause delays or terminations of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly obtain, maintain, enforce, defend or protect our intellectual property or proprietary rights or may use our proprietary information in such a way as to potentially lead to disputes or legal proceedings that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- disputes may arise with respect to the ownership of intellectual property developed pursuant to our collaborations;

- collaborators may infringe, misappropriate or otherwise violate the intellectual property or proprietary rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated for the convenience of the collaborator, and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner, or at all. If any collaborations that we enter into do not result in the successful development and commercialization of products or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, our development of our product candidates could be delayed and we may need additional resources to develop our product candidates. All of the risks relating to product development, regulatory approval and commercialization described in this prospectus also apply to the activities of our collaborators.

Additionally, subject to its contractual obligations to us, if a collaborator of ours is involved in a business combination, the collaborator might deemphasize or terminate the development or commercialization of any product candidate licensed to it by us. If one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our perception in the business and financial communities could be adversely affected.

If we are not able to establish or maintain collaborations, we may have to alter our development and commercialization plans and our business could be adversely affected.

For some of our product candidates, we may decide to collaborate with pharmaceutical or biotechnology companies for the development and potential commercialization of those product candidates. We face significant competition in seeking appropriate collaborators, and a number of more established companies may also be pursuing strategies to license or acquire third-party intellectual property rights that we consider attractive. These established companies may have a competitive advantage over us due to their size, financial resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. We are also restricted by GSK's right of first negotiation under our current license agreement with them and may in the future be restricted under other license agreements from entering into agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical and biotechnology companies that have resulted in a reduced number of potential future collaborators.

If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms or at all, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or

reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market or continue to develop our product engine.

Risks Related to our Intellectual Property

If we are unable to obtain, maintain, enforce and protect patent protection for our technology and product candidates or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully develop and commercialize our technology and product candidates may be adversely affected.

Our success depends in large part on our ability to obtain and maintain protection of the intellectual property we may own solely and jointly with others or may license from others, particularly patents, in the United States and other countries with respect to any proprietary technology and product candidates we develop. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our product candidates that are important to our business and by in-licensing intellectual property related to our technologies and product candidates. If we are unable to obtain or maintain patent protection with respect to any proprietary technology or product candidate, our business, financial condition, results of operations and prospects could be materially harmed.

The patent prosecution process is expensive, time-consuming and complex, and we may not be able to file, prosecute, maintain, defend or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain, enforce and defend the patents, covering technology that we license from third parties. Therefore, these in-licensed patents and applications may not be prepared, filed, prosecuted, maintained, defended and enforced in a manner consistent with the best interests of our business.

The patent position of pharmaceutical and biotechnology companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the scope of patent protection outside of the United States is uncertain and laws of foreign countries may not protect our rights to the same extent as the laws of the United States or vice versa. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does. With respect to both owned and in-licensed patent rights, we cannot predict whether the patent applications we and our licensors are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors. Further, we may not be aware of all third-party intellectual property rights potentially relating to our product candidates. In addition, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not published at all. Therefore, neither we nor our licensors can know with certainty whether either we or our licensors were the first to make the inventions claimed in the patents and patent applications we own or in-license now or in the future, or that either we or our licensors were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our owned and in-licensed patent rights are highly uncertain. Moreover, our owned and in-licensed pending and future patent applications may not result in patents being issued which protect our technology and product candidates, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in

either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents and our ability to obtain, protect, maintain, defend and enforce our patent rights, narrow the scope of our patent protection and, more generally, could affect the value or narrow the scope of our patent rights.

Currently, our patent portfolio related to FTX-HbF is in its earliest stages, including only provisional patent applications which do not themselves issue as patents. We have no issued patents related to FTX-HbF or our SCD or b-thalassemia programs. In order to continue to pursue protection based on provisional patent applications, we will need to file Patent Cooperation Treaty applications, foreign applications and/or U.S. non-provisional patent applications prior to applicable deadlines. Even then, as highlighted above, patents may never issue from our patent applications, or the scope of any patent may not be sufficient to provide a competitive advantage. With respect to losmapimod, the patents to losmapimod licensed from GSK as a composition of matter and pharmaceutical composition are expected to expire on February 10, 2023. Our owned patent applications are not to the composition but, rather, are directed to certain methods of treating FSHD. We cannot be certain that any patents will be granted in respect of these patent applications. Even if such patent applications issue as patents, they will not prevent third parties from commercializing losmapimod for other indications.

Moreover, we or our licensors may be subject to a third-party preissuance submission of prior art to the United States Patent and Trademark Office, or USPTO, or become involved in opposition, derivation, revocation, reexamination, *inter partes* review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize drugs without infringing third-party patent rights. If the breadth or strength of protection provided by our patents and patent applications is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Additionally, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if our owned and in-licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and in-licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and product candidates. Such proceedings also may result in substantial cost and require significant time from our management and employees, even if the eventual outcome is favorable to us. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. Furthermore, our competitors may be able to circumvent our owned or in-licensed patents by developing similar or alternative technologies or products in a non-infringing manner. As a result, our owned and in-licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing technology and products similar or identical to any of our technology and product candidates.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products, including generics or biosimilars. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. For example, the composition of matter patents covering losmapimod, licensed from GSK, are expected to expire on February 10, 2023. Given the near term expiration date of these patents, and the fact that safe harbor protections in many jurisdictions permit third parties to engage in development, including clinical trials, these patents may not provide us with any meaningful competitive advantage.

If we are unable to obtain licenses from third parties on commercially reasonable terms or fail to comply with our obligations under such agreements, our business could be harmed.

It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our products, in which case we would be required to obtain a license from these third parties. If we are unable to license such technology, or if we are forced to license such technology on unfavorable terms, our business could be materially harmed. If we are unable to obtain a necessary license, we may be unable to develop or commercialize the affected product candidates, which could materially harm our business and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales or an obligation on our part to pay royalties and/or other forms of compensation. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us.

If we are unable to obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may be required to expend significant time and resources to redesign our technology, product candidates, or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected technology and product candidates, which could harm our business, financial condition, results of operations and prospects significantly.

Additionally, if we fail to comply with our obligations under license agreements, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market, or may be forced to cease developing, manufacturing or marketing, any product that is covered by these agreements or may face other penalties under such agreements. Such an occurrence could materially adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements, or restrictions on our ability to freely assign or sublicense our rights under such agreements when it is in the interest of our business to do so, may result in our having to negotiate new or reinstated agreements with less favorable terms, cause us to lose our rights under these agreements, including our rights to important intellectual property or technology or impede, or delay or prohibit the further development or commercialization of one or more product candidates that rely on such agreements.

If we do not obtain patent term extension in the United States under the Hatch-Waxman Act and in foreign countries under similar legislation, thereby potentially extending the term of our marketing exclusivity for any product candidates we may develop, our business may be materially harmed.

In the United States, the patent term of a patent that covers an FDA-approved drug may be eligible for limited patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, and only one patent applicable to an approved drug may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Similar provisions are available in Europe and certain other non-United States jurisdictions to extend the term of a patent that covers an approved drug. While, in the future, if and when our product candidates receive FDA approval, we expect to apply for patent term extensions on patents covering those product candidates, there is no guarantee that the applicable authorities will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions. We may not be granted patent term extension either in the United States or in any foreign country because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the term of extension, as well as the scope of patent protection during any such extension, afforded by the governmental authority could be less than we request. If we are unable to obtain any patent term extension or the term of any such extension is less than we request, our competitors may obtain approval of competing products following the expiration of our patent rights, and our business, financial condition, results of operations and prospects could be materially harmed.

It is possible that we will not obtain patent term extension under the Hatch-Waxman Act for a U.S. patent covering any of our product candidates that we may identify even where that patent is eligible for patent term extension, or if we obtain such an extension, it may be for a shorter period than we had sought. Further, for our licensed patents, we may not have the right to control prosecution, including filing with the USPTO a petition for patent term extension under the Hatch-Waxman Act. Thus, if one of our licensed patents is eligible for patent term extension under the Hatch-Waxman Act, we may not be able to control whether a petition to obtain a patent term extension is filed, or obtained, from the USPTO.

Also, there are detailed rules and requirements regarding the patents that may be submitted to the FDA for listing in the Approved Drug Products with Therapeutic Equivalence Evaluations, or the Orange Book. We may be unable to obtain patents covering our product candidates that contain one or more claims that satisfy the requirements for listing in the Orange Book. Even if we submit a patent for listing in the Orange Book, the FDA may decline to list the patent, or a manufacturer of generic drugs may challenge the listing. If one of our product candidates is approved and a patent covering that product candidate is not listed in the Orange Book, a manufacturer of generic drugs would not have to provide advance notice to us of any abbreviated new drug application filed with the FDA to obtain permission to sell a generic version of such product candidate.

Changes to patent laws in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

Changes in either the patent laws or interpretation of patent laws in the United States, including patent reform legislation such as the Leahy-Smith America Invents Act, or the Leahy-Smith Act, could increase the uncertainties and costs surrounding the prosecution of our owned and in-licensed patent applications and the maintenance, enforcement or defense of our owned and in-licensed issued patents.

The Leahy-Smith Act includes a number of significant changes to United States patent law. These changes include provisions that affect the way patent applications are prosecuted, redefine prior art, provide more efficient and cost-effective avenues for competitors to challenge the validity of patents, and enable third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent at USPTO-administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings. Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith Act, the United States transitioned to a first-to-file system in which, assuming that the other statutory requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. As such, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our patent rights and our ability to protect, defend and enforce our patent rights in the future.

Although we or our licensors are not currently involved in any litigation, we may become involved in lawsuits to protect or enforce our patent or other intellectual property rights, which could be expensive, time-consuming and unsuccessful.

Competitors and other third parties may infringe, misappropriate or otherwise violate our or our licensor's issued patents or other intellectual property. As a result, we or our licensors may need to file infringement, misappropriation or other intellectual property related claims, which can be expensive and time-consuming. Any claims we assert against perceived infringers could provoke such parties to assert counterclaims against us alleging that we infringe, misappropriate or otherwise violate their intellectual property. In addition, in a patent infringement proceeding, such parties could counterclaim that the patents we or our licensors have asserted are invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Third parties may institute such claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). The outcome following legal assertions of invalidity and unenforceability is unpredictable.

An adverse result in any such proceeding could put one or more of our owned or in-licensed patents at risk of being invalidated or interpreted narrowly, and could put any of our owned or in-licensed patent applications at risk of not yielding an issued patent. A court may also refuse to stop the third party from using the technology at issue in a proceeding on the grounds that our owned or in-licensed patents do not cover such technology. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information or trade secrets could be compromised by disclosure during this type of litigation. Any of the foregoing could allow such third parties to develop and commercialize competing technologies and products and have a material adverse impact on our business, financial condition, results of operations and prospects.

Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all, or if a non-exclusive license is offered and our competitors gain access to the same technology. Our defense of litigation or interference or derivation proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties, or enter into development partnerships that would help us bring our product candidates to market.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

Third parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property and proprietary rights of third parties. There is considerable patent and other intellectual property litigation in the pharmaceutical and biotechnology industries. We may become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our technology and product candidates, including interference proceedings, post grant review, *inter partes* review, and derivation proceedings before the USPTO and similar proceedings in foreign jurisdictions such as oppositions before the European Patent Office. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are pursuing development candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our technologies or product candidates that we may identify may be subject to claims of infringement of the patent rights of third parties.

The legal threshold for initiating litigation or contested proceedings is low, so that even lawsuits or proceedings with a low probability of success might be initiated and require significant resources to defend. Litigation and contested proceedings can also be expensive and time-consuming, and our adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we can. The risks of being involved in such litigation and proceedings may increase if and as our product candidates near commercialization and as we gain the greater visibility associated with being a public company. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of merit. We may not be aware of all such intellectual property rights potentially relating to our technology and product candidates and their uses, or we may incorrectly conclude that third party intellectual property is invalid or that our activities and product candidates do not infringe such intellectual property. Thus, we do not know with certainty that our technology and product candidates, or our development and commercialization thereof, do not and will not infringe, misappropriate or otherwise violate any third party's intellectual property.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, formulations or methods,

such as methods of manufacture or methods for treatment, related to the discovery, use or manufacture of the product candidates that we may identify or related to our technologies. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that the product candidates that we may identify may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Moreover, as noted above, there may be existing patents that we are not aware of or that we have incorrectly concluded are invalid or not infringed by our activities. If any third-party patents were held by a court of competent jurisdiction to cover, for example, the manufacturing process of the product candidates that we may identify, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize the product candidates that we may identify. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

We may choose to take a license or, if we are found to infringe, misappropriate or otherwise violate a third party's intellectual property rights, we could also be required to obtain a license from such third party to continue developing, manufacturing and marketing our technology and product candidates. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us and could require us to make substantial licensing and royalty payments. We could be forced, including by court order, to cease developing, manufacturing and commercializing the infringing technology or product. In addition, we could be found liable for significant monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right and could be forced to indemnify our customers or collaborators. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. In addition, we may be forced to redesign our product candidates, seek new regulatory approvals and indemnify third parties pursuant to contractual agreements. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar material adverse effect on our business, financial condition, results of operations and prospects.

Intellectual property litigation or other legal proceedings relating to intellectual property could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and may also have an advantage in such proceedings due to their more mature and developed intellectual property portfolios. Uncertainties

resulting from the initiation and continuation of intellectual property litigation or other proceedings could compromise our ability to compete in the marketplace.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance, renewal and annuity fees and various other government fees on any issued patent and pending patent application must be paid to the USPTO and foreign patent agencies in several stages or annually over the lifetime of our owned and in-licensed patents and patent applications. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In certain circumstances, we rely on our licensing partners to pay these fees to, or comply with the procedural and documentary rules of, the relevant patent agency. With respect to our patents, we rely on an annuity service, outside firms and outside counsel to remind us of the due dates and to make payment after we instruct them to do so. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, potential competitors might be able to enter the market with similar or identical products or technology. If we or our licensors fail to maintain the patents and patent applications covering our product candidates, it would have a material adverse effect on our business, financial condition, results of operations and prospects.

If we fail to comply with our obligations in our intellectual property licenses and funding arrangements with third parties, or otherwise experience disruptions to our business relationships with our licensors, we could lose intellectual property rights that are important to our business.

We are party to license and funding agreements, such as the GSK Agreement, that impose, and we may enter into additional licensing and funding arrangements with third parties that may impose, diligence, development and commercialization timelines, milestone payment, royalty, insurance and other obligations on us. Under our existing licensing and funding agreements, we are obligated to pay royalties on net product sales of product candidates or related technologies to the extent they are covered by the agreements. If we fail to comply with such obligations under current or future license and funding agreements, our counterparties may have the right to terminate these agreements or require us to grant them certain rights. Such an occurrence could materially adversely affect the value of any product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology, which would have a material adverse effect on our business, financial condition, results of operations and prospects. We also have licenses and agreements to certain technologies used in our product engine, all of which are non-exclusive. While we still face all of the risks described herein with respect to those agreements, we cannot prevent third parties from also accessing those technologies. In addition, our licenses may place restrictions on our future business opportunities. For example, under our license with GSK, GSK has certain rights of first negotiation if we wish to sublicense any of the patent or data rights licensed by GSK to us to a third party for use outside the United States. This may prevent or delay certain transactions, which could have an adverse effect on the development and commercialization of losmapimod and on our business.

Disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, the agreements under which we currently license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected technology and product candidates, which could have a material adverse effect on our business, financial conditions, results of operations and prospects.

Our current or future licensors may have relied on third-party consultants or collaborators or on funds from third parties such that our licensors are not the sole and exclusive owners of the patents and patent applications we in-license. If other third parties have ownership rights to patents or patent applications we in-license, they may be able to license such patents to our competitors, and our competitors could market competing products and technology. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects.

In spite of our best efforts, our licensors might conclude that we have materially breached our license agreements and might therefore terminate the license agreements, thereby removing our ability to develop and commercialize product candidates and technology covered by these license agreements. If these in-licenses are terminated, or if the underlying intellectual property fails to provide the intended exclusivity, competitors would have the freedom to seek regulatory approval of, and to market, products and technologies identical to ours. This could have a material adverse effect on our competitive position, business, financial condition, results of operations and prospects.

We may not be able to protect our intellectual property and proprietary rights throughout the world.

Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States, and even where such protection is nominally available, judicial and governmental enforcement of such intellectual property rights may be lacking. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection or licenses but

enforcement is not as strong as that in the United States. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our intellectual property and proprietary rights generally. In addition, certain jurisdictions do not protect to the same extent or at all inventions that constitute new methods of treatment.

Proceedings to enforce our intellectual property and proprietary rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We or our licensors may be subject to claims that former employees, collaborators or other third parties have an interest in our owned or in-licensed patents, trade secrets or other intellectual property as an inventor or co-inventor. For example, we or our licensors may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or our or our licensors' ownership of our owned or in-licensed patents, trade secrets or other intellectual property. If we or our licensors fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to our product candidates. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may be subject to claims by third parties asserting that our employees, consultants or contractors have wrongfully used or disclosed confidential information of third parties, or we have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees, consultants and contractors were previously employed at universities or other pharmaceutical or biotechnology companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and contractors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these individuals or we have used

or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims.

In addition, while it is our policy to require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our intellectual property assignment agreements with them may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial conditions, results of operations and prospects.

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could have a material adverse effect on our competitive business position and prospects. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products, which license may not be available on commercially reasonable terms, or at all, or such license may be non-exclusive. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our management and employees.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for our product candidates, we also rely on trade secrets and confidentiality agreements to protect our unpatented know-how, technology and other proprietary information, to maintain our competitive position, including certain aspects of our proprietary product engine. We seek to protect our trade secrets and other proprietary technology, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract research organizations, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants, but we cannot guarantee that we have entered into such agreements with each party that may have or has had access to our trade secrets or proprietary technology. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Detecting the disclosure or misappropriation of a trade secret and enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside of the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our competitive position would be materially and adversely harmed.

Intellectual property rights do not necessarily address all potential threats.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- portions of our product engine are protected by trade secrets, but much of our product engine is not protected by intellectual property, including patents, trade secrets and know-how, and we may not be able to develop, acquire or in-license any patentable technologies or other intellectual property related to the unprotected portions of our product engine;

- others may be able to make product candidates that are similar to ours but that are not covered by the claims of the patents that we own;
- we, or our license partners or current or future collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent applications that we license or may own in the future;
- we, or our license partners or current or future collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or in-licensed intellectual property rights;
- it is possible that our owned and in-licensed pending patent applications or those we may own or in-license in the future will not lead to issued patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we cannot ensure that any of our patents, or any of our pending patent applications, if issued, or those of our licensors, will include claims having a scope sufficient to protect our product candidates;
- we cannot ensure that any patents issued to us or our licensors will provide a basis for an exclusive market for our commercially viable product candidates or will provide us with any competitive advantages;
- we cannot ensure that our commercial activities or product candidates will not infringe upon the patents of others;
- we cannot ensure that we will be able to successfully commercialize our product candidates on a substantial scale, if approved, before the relevant patents that we own or license expire;
- we may not develop additional proprietary technologies that are patentable;
- the patents of others may harm our business; and
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations and prospects.

Risks Related to Regulatory Approval of our Product Candidates and Other Legal Compliance Matters

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our product candidates. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates and the activities associated with their development and commercialization, including design, testing, manufacture, packaging, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, export, import and adverse event reporting, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by the EMA and similar

regulatory authorities outside of the United States. Marketing approval of drugs in the United States requires the submission of a new drug application, or NDA, to the FDA and we are not permitted to market any drug candidate in the United States until we obtain approval from the FDA of the NDA for that product. An NDA must be supported by extensive clinical and preclinical data, as well as extensive information regarding pharmacology, chemistry, manufacturing and controls. We have not submitted an application for or received marketing approval for any of our product candidates in the United States or in any other jurisdiction.

We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party clinical research organizations or other third-party consultants or vendors to assist us in this process. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use. If any of our product candidates receives marketing approval, the accompanying label may limit the approved use of our drug, which could limit sales of the product.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

We may not be able to obtain or maintain orphan drug designation or exclusivity for our product candidates and, even if we do, that exclusivity may not prevent the FDA or the EMA from approving other competing products.

We plan to apply for orphan drug designation for FSHD in the United States and Europe, and we may seek orphan drug designation for our other current or future product candidates. Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the United States.

Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for the same drug for that time period. The applicable period is seven years in the United States and ten years in Europe. The exclusivity period in Europe can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or EMA determines that

the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because competing drugs containing a different active ingredient can be approved for the same condition. In addition, even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

On August 3, 2017, the U.S. Congress passed the FDA Reauthorization Act of 2017, or FDARA. FDARA, among other things, codified the FDA's pre-existing regulatory interpretation to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

A Fast Track designation by the FDA may not lead to a faster development or regulatory review or approval process.

We may seek Fast Track designation for some of our product candidates. If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for FDA Fast Track designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive Fast Track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program.

A Breakthrough Therapy designation by the FDA for our product candidates may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval.

We may seek a Breakthrough Therapy designation for some of our product candidates. A Breakthrough Therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs and biologics that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as breakthrough therapies by the FDA are also eligible for accelerated approval.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. Even if we receive Breakthrough Therapy designation, the receipt of such designation for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of

our product candidates qualify as breakthrough therapies, the FDA may later decide that the products no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Accelerated approval by the FDA, even if granted for our product candidates, may not lead to a faster development or regulatory review or approval process and it does not increase the likelihood that our product candidates will receive marketing approval.

We may seek approval of our product candidates using the FDA's accelerated approval pathway. A product may be eligible for accelerated approval if it treats a serious or life-threatening condition and generally provides a meaningful advantage over available therapies. In addition, it must demonstrate an effect on a biomarker efficacy endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit. The FDA or other applicable regulatory agency makes the determination regarding whether a biomarker efficacy endpoint is reasonably likely to predict long-term clinical benefit.

Prior to seeking such accelerated approval, we will seek feedback from the FDA and otherwise evaluate our ability to seek and receive such accelerated approval. As a condition of approval, the FDA may require that a sponsor of a drug or biologic product candidate receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. These confirmatory trials must be completed with due diligence and we may be required to evaluate different or additional endpoints in these post-marketing confirmatory trials. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

There can be no assurance that the FDA will agree with our biomarker efficacy endpoints or intermediate clinical endpoints, such as measuring DUX4-driven gene expression in muscle tissue biopsies or measuring the fraction of muscle tissue by replaced by fat, or that we will decide to pursue or submit an NDA for accelerated approval or any other form of expedited development, review or approval. Similarly, there can be no assurance that, after feedback from FDA, we will continue to pursue or apply for accelerated approval or any other form of expedited development, review or approval, even if we initially decide to do so. Furthermore, if we decide to submit an application for accelerated approval or under another expedited regulatory designation, there can be no assurance that such submission or application will be accepted or that any expedited review or approval will be granted on a timely basis, or at all.

Moreover, as noted above, for drugs granted accelerated approval, the FDA typically requires post-marketing confirmatory trials to evaluate the anticipated effect on IMM or other clinical benefit. These confirmatory trials must be completed with due diligence. We may be required to evaluate additional or different clinical endpoints in these post-marketing confirmatory trials. These confirmatory trials may require enrollment of more patients than we currently anticipate and will result in additional costs, which may be greater than the estimated costs we currently anticipate. The FDA may withdraw approval of a product candidate approved under the accelerated approval pathway if, for example, the trial required to verify the predicted clinical benefit of our product candidate fails to verify such benefit or does not demonstrate sufficient clinical benefit to justify the risks associated with the drug. The FDA may also withdraw approval if other evidence demonstrates that our product candidate is not shown to be safe or effective under the conditions of use, we fail to conduct any required post approval trial of our product candidate with due diligence or we disseminate false or misleading promotional materials relating to our product candidate. A failure to obtain accelerated approval or any other form of expedited development, review or approval for our product candidates, or withdrawal of a product candidate, would result in a longer time period for commercialization of such product candidate, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace.

Even if we do receive accelerated approval, we may not experience a faster development or regulatory review or approval process, and receiving accelerated approval does not provide assurance of ultimate FDA approval.

Failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed abroad.

In order to market and sell our products in the European Union and many other foreign jurisdictions, we or our potential third-party collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside of the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside of the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We or our potential third-party collaborators may not obtain approvals from regulatory authorities outside of the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside of the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in other countries. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market.

Additionally, on June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. On March 29, 2017, the United Kingdom formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. The United Kingdom had a period of a maximum of two years from the date of its formal notification to negotiate the terms of its withdrawal from, and future relationship with, the European Union. If no formal withdrawal agreement can be reached between the United Kingdom and the European Union, then it is expected that the United Kingdom's membership of the European Union would automatically terminate on the deadline, which was initially March 29, 2019. That deadline has been extended to October 31, 2019 to allow the parties to negotiate a withdrawal agreement, which has proven to be extremely difficult to date. Discussions between the United Kingdom and the European Union will continue to focus on withdrawal issues and transition agreements. However, limited progress to date in these negotiations and ongoing uncertainty within the government of the United Kingdom sustains the possibility of the United Kingdom leaving the European Union without a withdrawal agreement and associated transition period in place, which is likely to cause significant market and economic disruption.

Since a significant proportion of the regulatory framework in the United Kingdom is derived from European Union directives and regulations, Brexit could materially impact the regulatory regime with respect to the approval of our product candidates in the United Kingdom or the European Union. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for our product candidates, which could significantly and materially harm our business.

Any product candidate for which we obtain marketing approval could be subject to post-marketing restrictions or withdrawal from the market and we may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including the requirement to implement a REMS. If any of our product candidates receives marketing approval, the accompanying label may limit the approved use of our drug, which could limit sales of the product.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product, including the adoption and implementation of REMS. The FDA and other agencies, including the Department of Justice, or the DOJ, closely regulate and monitor the post-approval marketing and promotion of drugs to ensure they are marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and DOJ impose stringent restrictions on manufacturers' communications regarding off-label use, and if we do not market our products for their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the Federal Food, Drug and Cosmetic Act, or FDCA, and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations and enforcement actions alleging violations of federal and state healthcare fraud and abuse laws, as well as state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may have various consequences, including:

- suspension of or restrictions on such products, manufacturers or manufacturing processes;
- restrictions and warnings on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension of any ongoing clinical trials;
- suspension or withdrawal of marketing approvals;
- damage to relationships with any potential collaborators;

- unfavorable press coverage and damage to our reputation;
- refusal to permit the import or export of our products;
- product seizure or detention;
- injunctions or the imposition of civil or criminal penalties; or
- litigation involving patients using our products.

Non-compliance with European Union requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with the European Union's requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs applicable to drug manufacturers or quality assurance standards applicable to medical device manufacturers, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, any contract manufacturers we may engage in the future, our future collaborators and their contract manufacturers will also be subject to other regulatory requirements, including submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements regarding the distribution of samples to clinicians, recordkeeping, and costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product such as the requirement to implement a REMS.

The efforts of the Trump administration to pursue regulatory reform may limit the FDA's ability to engage in oversight and implementation activities in the normal course, and that could negatively impact our business.

The Trump administration has taken several executive actions, including the issuance of a number of executive orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. On January 30, 2017, President Trump issued an executive order, applicable to all executive agencies, including the FDA, requiring that for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency shall identify at least two existing regulations to be repealed, unless prohibited by law. These requirements are referred to as the "two-for-one" provisions. This executive order includes a budget neutrality provision that requires the total incremental cost of all new regulations in the 2017 fiscal year, including repealed regulations, to be no greater than zero, except in limited circumstances. For fiscal years 2018 and beyond, the executive order requires agencies to identify regulations to offset any incremental cost of a new regulation. In interim guidance issued by the Office of Information and Regulatory Affairs within the Office of Management and on February 2, 2017, the Trump administration indicates that the "two-for-one" provisions may apply not only to agency regulations, but also to significant agency guidance documents. It is difficult to predict how these requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

Our relationships with healthcare providers, physicians and third-party payors will be subject to applicable anti-kickback, fraud and abuse, false claims, transparency, health information privacy and security, and other healthcare laws and regulations, which, in the event of a violation, could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings.

If we obtain regulatory approval and commercialize any products, healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with healthcare providers, physicians and third-party payors may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any products for which we obtain marketing approval. In addition, we may be subject to transparency laws and patient privacy regulation by U.S. federal and state governments and by governments in foreign jurisdictions in which we conduct our business. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;
- the federal False Claims Act imposes criminal and civil penalties, including through civil whistleblower or *qui tam* actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties, currently set at \$5,500 to \$11,000 per false claim;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, and their respective implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the FDCA, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices;
- the federal Physician Payments Sunshine Act requires applicable manufacturers of covered drugs to report payments and other transfers of value to physicians and teaching hospitals; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws and transparency statutes, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. Additionally,

some state and local laws require the registration of pharmaceutical sales representatives in the jurisdiction. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations, including anticipated activities that would be conducted by our sales team, are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from participation in government funded healthcare programs.

Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. For example, the collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the European Union, including personal health data, is subject to the EU General Data Protection Regulation, or the GDPR, which took effect across all member states of the European Economic Area, or EEA, in May 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR increases our obligations with respect to clinical trials conducted in the EEA by expanding the definition of personal data to include coded data and requiring changes to informed consent practices and more detailed notices for clinical trial subjects and investigators. In addition, the GDPR also imposes strict rules on the transfer of personal data to countries outside the European Union, including the United States and, as a result, increases the scrutiny that clinical trial sites located in the EEA should apply to transfers of personal data from such sites to countries that are considered to lack an adequate level of data protection, such as the United States. The GDPR also permits data protection authorities to require destruction of improperly gathered or used personal information and/or impose substantial fines for violations of the GDPR, which can be up to four percent of global revenues or 20 million Euros, whichever is greater, and it also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR provides that EU member states may make their own further laws and regulations limiting the processing of personal data, including genetic, biometric or health data.

Given the breadth and depth of changes in data protection obligations, preparing for and complying with the GDPR's requirements is rigorous and time intensive and requires significant resources and a review of our technologies, systems and practices, as well as those of any third-party collaborators, service

providers, contractors or consultants that process or transfer personal data collected in the European Union. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities and increase our cost of doing business, and could lead to government enforcement actions, private litigation and significant fines and penalties against us and could have a material adverse effect on our business, financial condition or results of operations. Similarly, failure to comply with federal and state laws regarding privacy and security of personal information could expose us to fines and penalties under such laws. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business.

Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain for any products that are approved in the United States or foreign jurisdictions.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval. The pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by legislative initiatives. Current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any FDA approved product.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for any approved products. While the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA. Among the provisions of the ACA of potential importance to our business, including, without limitation, our ability to commercialize and the prices we may obtain for any of our product candidates that are approved for sale, are the following:

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, although this fee would not apply to sales of certain products approved exclusively for orphan indications;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- expansion of healthcare fraud and abuse laws, including the civil False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;

- a Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% point-of-sale discounts off negotiated prices;
- extension of manufacturers' Medicaid rebate liability;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- requirements to report certain financial arrangements with physicians and teaching hospitals;
- a requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in 2013 and, due to subsequent legislative amendments to the statute, will stay in effect through 2027 unless additional congressional action is taken, and the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Further, there have been several recent U.S. congressional inquiries and proposed state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products.

We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

With enactment of the TCJA, which was signed by the President on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, is effective as of 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause an estimated 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018, among other things, amends the ACA, effective January 1, 2019, to increase from 50% to 70% the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole".

The Trump administration has also taken executive actions to undermine or delay implementation of the ACA. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. One Executive Order directs federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. The second Executive Order terminates the cost-sharing subsidies that reimburse insurers under the ACA. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017.

In addition, the Centers for Medicare & Medicaid Services, or CMS, has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than \$12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. The effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and potentially our business, are not yet known. On November 30, 2018, CMS announced a proposed rule that would amend the Medicare Advantage and Medicare Part D prescription drug benefit regulations to reduce out of pocket costs for plan enrollees and allow Medicare plans to negotiate lower rates for certain drugs. Among other things, the proposed rule changes would allow Medicare Advantage plans to use pre authorization (PA) and step therapy (ST) for six protected classes of drugs, with certain exceptions; permit plans to implement PA and ST in Medicare Part B drugs; and change the definition of "negotiated prices" as well as add a definition of "price concession" in the regulations. It is unclear whether these proposed changes will be accepted, and if so, what effect such changes will have on our business. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

Further, on December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseparable feature of the ACA, and therefore because the mandate was repealed as part of the TCJA, the remaining provisions of the ACA are invalid as well. The Trump administration and CMS have both stated that the ruling will have no immediate effect, and on December 30, 2018 the same judge issued an order staying the judgment pending appeal. The Trump administration has recently represented to the Court of Appeals considering this judgment that it does not oppose the lower court's ruling. It is unclear how this decision and any subsequent appeals and other efforts to repeal and replace the ACA will impact the ACA and our business. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The costs of prescription pharmaceuticals have also been the subject of considerable discussion in the United States, and members of Congress and the Trump administration have stated that they will address such costs through new legislative and administrative measures. To date, there have been several recent U.S. congressional inquiries and proposed and enacted state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, the Trump administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. While any proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new

legislative and/or administrative measures to control drug costs. At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Specifically, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. For example, on May 11, 2018, the Trump administration issued a plan to lower drug prices. Under this blueprint for action, the Trump administration indicated that the Department of Health and Human Services, or HHS, will: take steps to end the gaming of regulatory and patent processes by drug makers to unfairly protect monopolies; advance biosimilars and generics to boost price competition; evaluate the inclusion of prices in drug makers' advertisements to enhance price competition; speed access to and lower the cost of new drugs by clarifying policies for sharing information between insurers and drug makers; avoid excessive pricing by relying more on value-based pricing by expanding outcome-based payments in Medicare and Medicaid; work to give Part D plan sponsors more negotiation power with drug makers; examine which Medicare Part B drugs could be negotiated for a lower price by Part D plans, and improving the design of the Part B Competitive Acquisition Program; update Medicare's drug-pricing dashboard to increase transparency; prohibit Part D contracts that include "gag rules" that prevent pharmacists from informing patients when they could pay less out-of-pocket by not using insurance; and require that Part D plan members be provided with an annual statement of plan payments, out-of-pocket spending, and drug price increases. More recently, on January 31, 2019, the HHS Office of Inspector General proposed modifications to the federal Anti-Kickback Statute discount safe harbor for the purpose of reducing the cost of drug products to consumers which, among other things, if finalized, will affect discounts paid by manufacturers to Medicare Part D plans, Medicaid managed care organizations and pharmacy benefit managers working with these organizations.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. Increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

Governments outside of the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In some countries, particularly the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

If we or any third-party manufacturers we engage now or in the future fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs or liabilities that could harm our business.

We and third-party manufacturers we engage now are, and any third-party manufacturers we may engage in the future will be, subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. Liability under certain environmental laws governing the release and cleanup of hazardous materials is joint and several and could be imposed without regard to fault. We also could incur significant costs associated with civil or criminal fines and penalties or become subject to injunctions limiting or prohibiting our activities for failure to comply with such laws and regulations.

Although we maintain general liability insurance as well as workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Further, with respect to the operations of our current and any future third-party contract manufacturers, it is possible that if they fail to operate in compliance with applicable environmental, health and safety laws and regulations or properly dispose of wastes associated with our products, we could be held liable for any resulting damages, suffer reputational harm or experience a disruption in the manufacture and supply of our product candidates or products. In addition, our supply chain may be adversely impacted if any of our third-party contract manufacturers become subject to injunctions or other sanctions as a result of their non-compliance with environmental, health and safety laws and regulations.

We are subject to anti-corruption laws, as well as export control laws, customs laws, sanctions laws and other laws governing our operations. If we fail to comply with these laws, we could be subject to civil or criminal penalties, other remedial measures and legal expenses, be precluded from developing manufacturing and selling certain products outside the United States or be required to develop and implement costly compliance programs, which could adversely affect our business, results of operations and financial condition.

Our operations are subject to anti-corruption laws, including the U.K. Bribery Act 2010, or Bribery Act, the U.S. Foreign Corrupt Practices Act, or FCPA, and other anti-corruption laws that apply in countries where we do business and may do business in the future. The Bribery Act, FCPA and these other laws generally prohibit us, our officers, and our employees and intermediaries from bribing, being bribed or making other prohibited payments to government officials or other persons to obtain or retain business or gain some other business advantage. Compliance with the FCPA, in particular, is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

We may in the future operate in jurisdictions that pose a high risk of potential Bribery Act or FCPA violations, and we may participate in collaborations and relationships with third parties whose actions could potentially subject us to liability under the Bribery Act, FCPA or local anti-corruption laws. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted. If we expand our operations outside of the United States, we will need to dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate.

We are also subject to other laws and regulations governing our international operations, including regulations administered by the governments of the United Kingdom and the United States, and authorities in the European Union, including applicable export control regulations, economic sanctions on countries and persons, customs requirements and currency exchange regulations, collectively referred to as the Trade Control laws. In addition, various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain products and product candidates outside of the United States, which could limit our growth potential and increase our development costs.

There is no assurance that we will be completely effective in ensuring our compliance with all applicable anti-corruption laws, including the Bribery Act, the FCPA or other legal requirements, including Trade Control laws. If we are not in compliance with the Bribery Act, the FCPA and other anti-corruption laws or Trade Control laws, we may be subject to criminal and civil penalties, disgorgement and other sanctions and remedial measures, and legal expenses, which could have an adverse impact on our business, financial condition, results of operations and liquidity. The Securities and Exchange Commission, or SEC, also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions. Any investigation of any potential violations of the Bribery Act, the FCPA, other anti-corruption laws or Trade Control laws by United Kingdom, U.S. or other authorities could also have an adverse impact on our reputation, our business, results of operations and financial condition.

Our employees, independent contractors, consultants and vendors may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of fraud or other misconduct by our employees, independent contractors, consultants and vendors. Misconduct by these partners could include intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide accurate information to the FDA or comparable foreign regulatory authorities, comply with manufacturing standards, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. This could include violations of HIPAA, other U.S. federal and state law, and requirements of non-U.S. jurisdictions, including the European Union Data Protection Directive. We are also exposed to risks in connection with any insider trading violations by employees or others affiliated with us. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards, regulations, guidance or codes of conduct. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

Our internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Our internal computer systems and those of any collaborators, contractors or consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Such systems are also vulnerable to service interruptions or to security breaches from inadvertent or intentional actions by our employees, third-party vendors and/or business partners, or from cyber-attacks by malicious third parties. Cyber-attacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyber-attacks could include the deployment of harmful malware, ransomware, denial-of-service attacks, unauthorized access to or deletion of files, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. For example, we make extensive use of cloud-based storage systems, and in October 2018, we experienced a breach of one such system. While this breach did not result in the permanent loss or theft of any of our critical information or any other material consequences, it could have, and while we took steps to remediate this breach, such as establishing multi-factor authentication and implementing improvements to our data securities protocols, we cannot guarantee that the measures we have taken to date, and actions we may take in the future, will be sufficient to remediate any future breaches. Cyber-attacks also could include phishing attempts or e-mail fraud to cause payments or information to be transmitted to an unintended recipient.

While we have not experienced any material system failure, accident, cyber-attack or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed and the further development and commercialization of our product candidates could be delayed.

Risks Related to Employee Matters and Managing Growth

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on the research and development, clinical, financial, operational and other business expertise of our executive officers, as well as the other principal members of our management, scientific and clinical teams. Although we have entered into employment offer letters with our executive officers, each of them may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees. Recruiting and retaining qualified scientific, clinical, manufacturing, accounting, legal and sales and marketing personnel will also be critical to our success.

The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. Our success as a public company also depends on implementing and maintaining internal controls and the accuracy and timeliness of our financial reporting. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

We expect to expand our development and regulatory capabilities and potentially implement sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, clinical, regulatory affairs and, if any of our product candidates receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Risks Related to our Common Stock

After this offering, our executive officers, directors and principal stockholders, if they choose to act together, will continue to have the ability to control all matters submitted to stockholders for approval.

Upon the closing of this offering, our executive officers and directors and our stockholders who owned more than 5% of our outstanding common stock before this offering will, in the aggregate, beneficially own shares representing approximately % of our capital stock. As a result, if these stockholders were to choose to act together, they would be able to control all matters submitted to our stockholders for

approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets.

This concentration of ownership control may:

- delay, defer or prevent a change in control;
- entrench our management and board of directors; or
- delay or prevent a merger, consolidation, takeover or other business combination involving us that other stockholders may desire.

Provisions in our corporate charter documents and under Delaware law could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current directors and members of management.

Provisions in our certificate of incorporation and our bylaws that will become effective upon the closing of this offering may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that only one of three classes of directors is elected each year;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from our board of directors;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal specified provisions of our certificate of incorporation or bylaws that will become effective upon the closing of this offering.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, or the DGCL, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

If you purchase shares of common stock in this offering, you will suffer immediate dilution of your investment.

The initial public offering price of our common stock will be substantially higher than the pro forma as adjusted net tangible book value per share of our common stock. Therefore, if you purchase shares of our common stock in this offering, you will pay a price per share that substantially exceeds our pro forma as adjusted net tangible book value per share after this offering. To the extent outstanding options are exercised, you will incur further dilution. Based on an assumed initial public offering price of \$ per share, which is the midpoint of the estimated price range set forth on the cover page of this prospectus, you will experience immediate dilution of \$ per share, representing the difference between our pro forma as adjusted net tangible book value per share, after giving effect to this offering, and the assumed initial public offering price.

An active trading market for our common stock may not develop.

Prior to this offering, there has been no public market for our common stock. The initial public offering price for our common stock will be determined through negotiations with the underwriters. Although we have applied to have our common stock approved for listing on the Nasdaq Global Market, an active trading market for our shares may never develop or be sustained following this offering. If an active market for our common stock does not develop, it may be difficult for you to sell shares you purchase in this offering without depressing the market price for the shares or at all.

If securities analysts do not publish or cease publishing research or reports or publish misleading, inaccurate or unfavorable research about our business or if they publish negative evaluations of our stock, the price and trading volume of our stock could decline.

The trading market for our common stock will rely, in part, on the research and reports that industry or financial analysts publish about us or our business. We do not currently have, and may never obtain, research coverage by industry or financial analysts. If no, or few, analysts commence coverage of us, the trading price of our stock would likely decrease. Even if we do obtain analyst coverage, if one or more of the analysts covering our business downgrade their evaluations of our stock or publish inaccurate or unfavorable research about our business, or provides more favorable relative recommendations about our competitors, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price and trading volume to decline.

The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock in this offering.

Our stock price is likely to be volatile. The stock market in general and the market for smaller biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your common stock at or above the initial public offering price. The market price for our common stock may be influenced by many factors, including:

- results of or developments in preclinical studies and clinical trials of our product candidates or those of our competitors or potential collaborators;
- our success in commercializing our product candidates, if and when approved;
- the success of competitive products or technologies;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other intellectual property or proprietary rights;

- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license products, product candidates, technologies or data referencing rights, the costs of commercializing any such products and the costs of development of any such product candidates or technologies;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or the financial results of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this "Risk Factors" section.

In the past, following periods of volatility in the market price of a company's securities, securities class-action litigation has often been instituted against that company. Any lawsuit to which we are a party, with or without merit, may result in an unfavorable judgment. We also may decide to settle lawsuits on unfavorable terms. Any such negative outcome could result in payments of substantial damages or fines, damage to our reputation or adverse changes to our offerings or business practices. Such litigation may also cause us to incur other substantial costs to defend such claims and divert management's attention and resources. Furthermore, negative public announcements of the results of hearings, motions or other interim proceedings or developments could have a negative effect on the market price of our common stock.

We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

A significant portion of our total outstanding shares are eligible to be sold into the market in the near future, which could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. After this offering, we will have _____ shares of common stock outstanding based on the number of shares outstanding as of _____, 2019. This includes the shares that we are selling in this offering, which may be resold in the public market immediately without restriction, unless purchased by our affiliates or existing stockholders. The remaining shares are currently restricted as a result of securities laws or lock-up agreements but will become eligible to be sold at various times after the offering. Moreover, beginning 180 days after the completion of this offering, holders of an aggregate of _____ shares of our common stock will have rights, along with holders of an additional _____ shares of our common stock issuable upon exercise of outstanding options, subject to specified conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We also intend to register all shares of

common stock that we may issue under our equity compensation plans. Once we register these shares, they can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and the lock-up agreements described in the "Underwriters" section of this prospectus.

We are an "emerging growth company," and the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors.

We are an "emerging growth company," or EGC, as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. We may remain an EGC until the end of the fiscal year in which the fifth anniversary of this offering occurs, although if the market value of our common stock that is held by non-affiliates exceeds \$700 million as of any June 30 before that time or if we have annual gross revenues of \$1.07 billion or more in any fiscal year, we would cease to be an EGC as of December 31 of the applicable year. We also would cease to be an EGC if we issue more than \$1 billion of non-convertible debt over a three-year period. For so long as we remain an EGC, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not EGCs. These exemptions include:

- being permitted to provide only two years of audited financial statements in this prospectus, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We have taken advantage of reduced reporting obligations in this prospectus. In particular, in this prospectus, we have provided only two years of audited financial statements and have not included all of the executive compensation related information that would be required if we were not an EGC.

We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

In addition, the JOBS Act permits an EGC to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have elected not to "opt out" of such extended transition period, which means that when a standard is issued or revised and it has different application dates for public or private companies, we will adopt the new or revised standard at the time private companies adopt the new or revised standard and will do so until such time that we either (i) irrevocably elect to "opt out" of such extended transition period or (ii) no longer qualify as an EGC.

We will incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, and particularly after we are no longer an EGC, we will incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of

2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the Nasdaq Global Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs, particularly as we hire additional financial and accounting employees to meet public company internal control and financial reporting requirements, and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified members of our board of directors.

We are evaluating these rules and regulations, and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we will be required to furnish a report by our management on our internal control over financial reporting. However, while we remain an EGC, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, including through hiring additional financial and accounting personnel, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses in our internal control over financial reporting, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

Our certificate of incorporation that will become effective upon the closing of this offering designates the state courts in the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could discourage lawsuits against the company and our directors, officers and employees.

Our certificate of incorporation that will become effective upon the closing of this offering provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if the Court of Chancery of the State of Delaware does not have jurisdiction, the federal district court for the District of Delaware) will be the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, employees or stockholders to our company or our

stockholders, (3) any action asserting a claim arising pursuant to any provision of the DGCL or as to which the DGCL confers jurisdiction on the Court of Chancery of the State of Delaware or (4) any action asserting a claim arising pursuant to any provision of our certificate of incorporation or bylaws (in each case, as they may be amended from time to time) or governed by the internal affairs doctrine. This exclusive forum provision will not apply to actions arising under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended.

This exclusive forum provision may limit the ability of our stockholders to bring a claim in a judicial forum that such stockholders find favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees. Alternatively, if a court were to find the choice of forum provision contained in our certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could materially adversely affect our business, financial condition and operating results.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This prospectus contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical fact, contained in this prospectus, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "continue" "could," "estimate," "expect," "intend," "may," "might," "plan," "potential," "predict," "project," "should," "target," "would," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this prospectus include, among other things, statements about:

- our ongoing Phase 1 clinical trial and planned Phase 2b clinical trial and Phase 2 open label clinical trial of losmapimod;
- our IND-enabling studies and planned Phase 1 clinical trial of FTX-HbF;
- the initiation, timing, progress and results of our drug target discovery screening programs;
- the initiation, timing, progress and results of our current and future preclinical studies and clinical trials and our research and development programs;
- our plans to develop and, if approved, subsequently commercialize losmapimod and any other product candidates, including in combination with other drugs and therapies;
- the timing of and our ability to submit applications for, obtain and maintain regulatory approvals for losmapimod and other product candidates;
- our expectations regarding our ability to fund our operating expenses and capital expenditure requirements with our cash and cash equivalents and proceeds of this offering;
- the potential advantages of our product candidates;
- the rate and degree of market acceptance and clinical utility of our products;
- our estimates regarding the potential market opportunity for our product candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position;
- our ability to identify additional products, product candidates or technologies with significant commercial potential that are consistent with our commercial objectives;
- our expectations related to the use of proceeds from this offering;
- our estimates regarding expenses, future revenue, timing of any future revenue, capital requirements and needs for additional financing;
- the impact of government laws and regulations;
- our competitive position;
- developments relating to our competitors and our industry;
- our ability to maintain and establish collaborations or obtain additional funding; and
- our expectations regarding the time during which we will be an emerging growth company under the JOBS Act.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or

events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this prospectus, particularly in the "Risk Factors" section, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, collaborations, joint ventures or investments we may make or enter into.

You should read this prospectus and the documents that we reference in this prospectus and have filed as exhibits to the registration statement of which this prospectus is a part completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements contained in this prospectus are made as of the date of this prospectus, and we do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by applicable law.

This prospectus includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties as well as our own estimates of potential market opportunities. All of the market data used in this prospectus involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our estimates of the potential market opportunities for our product candidates include several key assumptions based on our industry knowledge, industry publications, third-party research and other surveys, which may be based on a small sample size and may fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions.

USE OF PROCEEDS

We estimate that the net proceeds from our issuance and sale of _____ shares of our common stock in this offering will be approximately \$ _____ million, assuming an initial public offering price of \$ _____ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their option to purchase additional shares of our common stock in full, we estimate that the net proceeds from this offering will be approximately \$ _____ million.

A \$1.00 increase (decrease) in the assumed initial public offering price of \$ _____ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the net proceeds to us from this offering by approximately \$ _____ million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. An increase (decrease) of 1,000,000 shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase (decrease) the net proceeds to us from this offering by approximately \$ _____ million, assuming no change in the assumed initial public offering price per share and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

As of March 31, 2019, we had cash and cash equivalents of \$62.5 million. We currently estimate that we will use the net proceeds from this offering, together with our existing cash and cash equivalents, as follows:

- approximately \$ _____ million to advance losmapimod for FSHD;
- approximately \$ _____ million to advance our hemoglobinopathies program;
- approximately \$ _____ million to fund our ongoing product engine and discovery efforts; and
- the remainder for working capital and other general corporate purposes.

This expected use of net proceeds from this offering and our existing cash and cash equivalents represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development programs, the status of and results from clinical trials, the timing of regulatory submissions and the outcome of regulatory review, as well as any collaborations that we may enter into with third parties for our product candidates, and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering.

Based on our planned use of the net proceeds from this offering, together with our existing cash and cash equivalents, we estimate that such funds will be sufficient to fund our operating expenses and capital expenditure requirements into _____. We anticipate that the net proceeds from this offering together with our existing cash and cash equivalents will be sufficient to allow us to _____. We will require additional capital to advance losmapimod through additional clinical trials, if required, to advance FTX-HbF through necessary clinical trials and to commercialize any of our product candidates, if we receive regulatory approval. We have based these estimates on assumptions that may prove to be wrong, including assumptions regarding the clinical trials necessary for FDA approval of our product candidates, and we could use our capital resources sooner than we currently expect. Due to the numerous risks and uncertainties associated with product development, including the risks and uncertainties with respect to successful enrollment and completion of clinical trials, at this time, we cannot reasonably estimate the amount of additional funding that will be necessary to complete the clinical development of losmapimod or any future product candidates. If we receive regulatory approval for losmapimod or other product

candidates, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution.

Pending our use of the net proceeds from this offering, we intend to invest the net proceeds in a variety of capital preservation investments, including short-term, investment-grade, interest-bearing instruments and U.S. government securities.

DIVIDEND POLICY

We have never declared or paid cash dividends on our common stock. We currently intend to retain all available funds and any future earnings to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination to declare and pay dividends will be made at the discretion of our board of directors and will depend on then-existing conditions, including our results of operations, financial condition, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

CAPITALIZATION

The following table sets forth our cash and cash equivalents and our capitalization as of March 31, 2019:

- on an actual basis;
- on a pro forma basis to give effect to (i) the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 112,500,000 shares of common stock upon the closing of this offering and (ii) the filing and effectiveness of our certificate of incorporation; and
- on a pro forma as adjusted basis to give further effect to our issuance and sale of _____ shares of our common stock in this offering at an assumed initial public offering price of \$ _____ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The pro forma and pro forma as adjusted information below is illustrative only, and our capitalization following the completion of this offering will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing. You should read the information in this table together with our consolidated financial statements and the related notes appearing at the end of this prospectus and the "Selected Consolidated Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections of this prospectus.

	As of March 31, 2019		
	Actual	Pro Forma	Pro Forma As Adjusted
	(in thousands, except share and per share data)		
Cash and cash equivalents	\$ 62,452	\$ 62,452	\$ _____
Convertible preferred stock (Series A and B), \$0.001 par value; 112,500,000 shares authorized, issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	165,136	—	—
Stockholders' (deficit) equity			
Preferred stock, \$0.001 par value; no shares authorized, issued or outstanding, actual; 5,000,000 shares authorized, no shares issued or outstanding, pro forma and pro forma as adjusted	—	—	—
Common stock, \$0.001 par value; 147,500,000 shares authorized, 19,235,125 shares issued and 12,054,235 shares outstanding, actual; 200,000,000 shares authorized, 131,735,125 shares issued and 124,554,235 shares outstanding, pro forma; 200,000,000 shares authorized, _____ shares issued and _____ shares outstanding, pro forma as adjusted	12	125	_____
Additional paid-in capital	5,268	170,291	_____
Accumulated deficit	(104,967)	(104,967)	_____
Total stockholders' (deficit) equity	(99,687)	65,449	_____
Total capitalization	\$ 65,449	\$ 65,449	\$ _____

A \$1.00 increase (decrease) in the assumed initial public offering price of \$ _____ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash and cash equivalents, additional paid-in capital, total stockholders' equity and total capitalization by \$ _____ million, assuming that the number of shares

offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. An increase (decrease) of 1,000,000 shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash and cash equivalents, common stock, additional paid-in capital, total stockholders' equity and total capitalization by \$ _____ million, assuming no change in the assumed initial public offering price per share and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The table above does not include:

- 10,698,963 shares of common stock issuable upon the exercise of stock options outstanding as of March 31, 2019, at a weighted average exercise price of \$1.09 per share, and an additional 658,000 shares of common stock issuable upon the exercise of stock options granted subsequent to March 31, 2019, at a weighted average exercise price of \$1.58 per share;
- 2,565,912 shares of common stock available for future issuance as of March 31, 2019 under our 2016 Stock Incentive Plan, as amended, or the 2016 Plan; and
- 14,120,000 and 1,765,000 additional shares of our common stock that will become available for future issuance under our 2019 Stock Incentive Plan, of which our board of directors has granted options to purchase an aggregate of 2,159,544 shares of common stock to certain of our employees and non-employee directors effective upon the commencement of trading of our common stock on the Nasdaq Stock Market, and our 2019 Employee Stock Purchase Plan, respectively, each of which will become effective immediately prior to the effectiveness of the registration statement of which this prospectus is a part, as well as any automatic increases in the number of shares of common stock reserved for future issuance under these plans.

DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted immediately to the extent of the difference between the initial public offering price per share of our common stock and the pro forma as adjusted net tangible book value per share of our common stock immediately after this offering.

Our historical net tangible book value (deficit) as of March 31, 2019 was \$(99.9) million, or \$(5.19) per share of common stock. Our historical net tangible book value (deficit) is the amount of our total tangible assets less our total liabilities and the carrying value of our preferred stock, which is not included within stockholders' (deficit) equity. Historical net tangible book value (deficit) per share represents historical net tangible book value (deficit) divided by the 19,235,125 shares of common stock outstanding as of March 31, 2019, including 7,180,890 shares of unvested restricted stock subject to repurchase by us.

Our pro forma net tangible book value as of March 31, 2019 was \$65.3 million, or \$0.50 per share of common stock. Pro forma net tangible book value represents the amount of our total tangible assets less our total liabilities, after giving effect to the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 112,500,000 shares of common stock upon the closing of this offering. Pro forma net tangible book value per share represents pro forma net tangible book value divided by the total number of shares outstanding as of March 31, 2019, after giving effect to the pro forma adjustments described above.

After giving further effect to our issuance and sale of _____ shares of our common stock in this offering at an assumed initial public offering price of \$ _____ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of March 31, 2019 would have been \$ _____ million, or \$ _____ per share. This represents an immediate increase in pro forma as adjusted net tangible book value per share of \$ _____ to existing stockholders and immediate dilution of \$ _____ in pro forma as adjusted net tangible book value per share to new investors purchasing shares of common stock in this offering. Dilution per share to new investors is determined by subtracting pro forma as adjusted net tangible book value per share after this offering from the assumed initial public offering price per share paid by new investors. The following table illustrates this dilution on a per share basis:

Assumed initial public offering price per share	
Historical net tangible book value (deficit) per share as of March 31, 2019	\$ (5.19)
Increase per share attributable to the pro forma adjustments described above	5.69
Pro forma net tangible book value per share as of March 31, 2019	\$ 0.50
Increase in pro forma as adjusted net tangible book value per share attributable to new investors purchasing shares of common stock in this offering	_____
Pro forma as adjusted net tangible book value per share immediately after this offering	_____
Dilution per share to new investors purchasing shares of common stock in this offering	_____

The dilution information discussed above is illustrative only and will change based on the actual initial public offering price and other terms of this offering determined at pricing. A \$1.00 increase (decrease) in the assumed initial public offering price of \$ _____ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) our pro forma as adjusted net tangible book value per share after this offering by \$ _____ and dilution per share to new investors purchasing shares of common stock in this offering by \$ _____, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting

estimated underwriting discounts and commissions and estimated offering expenses payable by us. An increase of 1,000,000 shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase our pro forma as adjusted net tangible book value per share after this offering by \$ _____ and decrease the dilution per share to new investors purchasing shares of common stock in this offering by \$ _____, assuming no change in the assumed initial public offering price per share and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. A decrease of 1,000,000 shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would decrease our pro forma as adjusted net tangible book value per share after this offering by \$ _____ and increase the dilution per share to new investors purchasing shares of common stock in this offering by \$ _____, assuming no change in the assumed initial public offering price and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

If the underwriters exercise their option to purchase additional shares in full, our pro forma as adjusted net tangible book value per share after this offering would be \$ _____, representing an immediate increase in pro forma as adjusted net tangible book value per share of \$ _____ to existing stockholders and immediate dilution in pro forma as adjusted net tangible book value per share of \$ _____ to new investors purchasing shares of common stock in this offering, assuming an initial public offering price of \$ _____ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The following table summarizes, as of March 31, 2019, on the pro forma as adjusted basis described above, the total number of shares of common stock purchased from us on an as converted to common stock basis, the total consideration paid or to be paid and the average price per share paid or to be paid by existing stockholders and by new investors in this offering at an assumed initial public offering price of \$ _____ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, before deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. As the table shows, new investors purchasing shares of common stock in this offering will pay an average price per share substantially higher than our existing stockholders paid.

	<u>Shares Purchased</u>		<u>Total Consideration</u>		<u>Average Price</u>
	<u>Number</u>	<u>Percent</u>	<u>Amount</u>	<u>Percentage</u>	<u>Per Share</u>
Existing stockholders					\$
Investors purchasing shares of common stock in this offering		%			/\$
Total		100%		100%	

A \$1.00 increase (decrease) in the assumed initial public offering price of \$ _____ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the total consideration paid by new investors by \$ _____ million and, in the case of an increase, would increase the percentage of total consideration paid by new investors by _____ percentage points and, in the case of a decrease, would decrease the percentage of total consideration paid by new investors by _____ percentage points, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same. An increase (decrease) of 1,000,000 shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase (decrease) the total consideration paid by new investors by \$ _____ million and, in the case of an increase, would increase the percentage of total consideration paid by new investors by _____ percentage points and, in the case of a decrease, would decrease the percentage of total consideration paid by new investors by _____ percentage points, assuming no change in the assumed initial public offering price.

The table above assumes no exercise of the underwriters' option to purchase additional shares in this offering. If the underwriters exercise their option to purchase additional shares in full, the number of shares of our common stock held by existing stockholders would be reduced to _____ % of the total number of shares of our common stock outstanding after this offering, and the number of shares of common stock held by new investors purchasing shares of common stock in this offering would be increased to _____ % of the total number of shares of our common stock outstanding after this offering.

The tables and discussion above are based on 19,235,125 shares of our common stock outstanding as of March 31, 2019, including 7,180,890 shares of unvested restricted stock subject to repurchase by us, and exclude:

- 10,698,963 shares of common stock issuable upon the exercise of stock options outstanding as of March 31, 2019, at a weighted average exercise price of \$1.09 per share, and an additional 658,000 shares of common stock issuable upon the exercise of stock options granted subsequent to March 31, 2019, at a weighted average exercise price of \$1.58 per share;
- 2,565,912 shares of common stock available for future issuance as of March 31, 2019 under our 2016 Plan; and
- 14,120,000 and 1,765,000 additional shares of our common stock that will become available for future issuance under our 2019 Stock Incentive Plan, of which our board of directors has granted options to purchase an aggregate of 2,159,544 shares of common stock to certain of our employees and non-employee directors effective upon the commencement of trading of our common stock on the Nasdaq Stock Market, and our 2019 Employee Stock Purchase Plan, respectively, each of which will become effective immediately prior to the effectiveness of the registration statement of which this prospectus is a part, as well as any automatic increases in the number of shares of common stock reserved for future issuance under these plans.

To the extent that outstanding stock options are exercised, new stock options are issued, or we issue additional shares of common stock in the future, there will be further dilution to investors purchasing shares of common stock in this offering. In addition, we may choose to raise additional capital because of market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. If we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

SELECTED CONSOLIDATED FINANCIAL DATA

You should read the following selected consolidated financial data together with our consolidated financial statements and the related notes appearing at the end of this prospectus and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of this prospectus. We have derived the consolidated statement of operations data for the years ended December 31, 2017 and 2018 and the consolidated balance sheet data as of December 31, 2017 and 2018 from our annual consolidated financial statements appearing at the end of this prospectus. The consolidated statement of operations data for the three months ended March 31, 2018 and 2019 and the consolidated balance sheet data as of March 31, 2019 have been derived from our interim consolidated financial statements appearing at the end of this prospectus and have been prepared on the same basis as the annual consolidated financial statements. In the opinion of management, the interim data reflect all normal recurring adjustments necessary for the fair presentation of the financial information in those statements. Our historical results are not necessarily indicative of the results that may be expected in the future, and our results for any interim period are not necessarily indicative of the results that should be expected for any full year or any other period.

	Year Ended December 31,		Three Months Ended March 31,	
	2017	2018	2018	2019
(in thousands, except per share data)				
Consolidated Statement of Operations Data:				
Operating expenses:				
Research and development	\$ 18,494	\$ 25,184	\$ 5,573	\$ 34,629
General and administrative	4,499	8,314	1,737	2,598
Total operating expenses	22,993	33,498	7,310	37,227
Loss from operations	(22,993)	(33,498)	(7,310)	(37,227)
Other income, net:				
Interest income, net	1	518	—	377
Other income	28	392	370	7
Net loss and comprehensive loss	\$ (22,964)	\$ (32,588)	\$ (6,940)	\$ (36,843)
Cumulative convertible preferred stock dividends	\$ (2,407)	\$ (6,559)	(828)	(3,041)
Net loss attributable to common stockholders	\$ (25,371)	\$ (39,147)	\$ (7,768)	\$ (39,884)
Net loss per share attributable to common stockholders, basic and diluted ⁽¹⁾	\$ (5.09)	\$ (4.45)	\$ (1.09)	\$ (3.47)
Weighted average number of common shares used in net loss per share attributable to common stockholders, basic and diluted ⁽¹⁾	4,980	8,799	7,134	11,497
Pro forma net loss per share attributable to common stockholders, basic and diluted ⁽¹⁾		\$ (0.43)		\$ (0.31)
Pro forma weighted average number of common shares used in net loss per share attributable to common stockholders, basic and diluted ⁽¹⁾		76,655		118,580

- (1) See Note 12 to our annual and interim consolidated financial statements appearing at the end of this prospectus for details on the calculation of basic and diluted net loss per share attributable to common stockholders and unaudited basic and diluted pro forma net loss per share attributable to common stockholders.

	<u>As of December 31,</u>		<u>As of</u>
	<u>2017</u>	<u>2018</u>	<u>March 31,</u>
		(in thousands)	2019
Consolidated Balance Sheet Data:			
Cash and cash equivalents	\$ 407	\$ 72,797	\$ 62,452
Working (deficit) capital ⁽¹⁾	(1,447)	69,866	59,306
Total assets	4,340	85,771	75,588
Convertible preferred stock	34,587	139,670	165,136
Total stockholders' deficit	(33,265)	(63,670)	(99,687)

(1) We define working (deficit) capital as current assets less current liabilities.

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with the "Selected Consolidated Financial Data" section of this prospectus and our consolidated financial statements and related notes appearing at the end of this prospectus. Some of the information contained in this discussion and analysis or set forth elsewhere in this prospectus, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this prospectus, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a clinical-stage biopharmaceutical company focused on improving the lives of patients with genetically defined diseases in areas of high unmet medical need, with an initial focus on rare diseases. We have developed a proprietary product engine that we employ to systematically identify and validate cellular drug targets that can potentially modulate gene expression to treat the known root cause of genetically defined diseases. We are using our product engine to identify targets that can be drugged by small molecules regardless of the particular underlying mechanism of gene mis-expression. We have identified drug targets to treat the root causes of facioscapulohumeral muscular dystrophy, or FSHD, and certain hemoglobinopathies, namely sickle cell disease, or SCD, and β -thalassemia. We expect to initiate a Phase 2b clinical trial of losmapimod, our product candidate for FSHD, in mid-2019. We commenced a Phase 1 clinical trial in February 2019 to obtain safety and tolerability data for losmapimod in patients with FSHD. We plan to submit an investigational new drug application, or IND, for FTX-HbF, our product candidate for certain hemoglobinopathies, in mid-2020.

Since inception, our operations have focused on organizing and staffing our company, business planning, raising capital, establishing our intellectual property, building our discovery platform, including our proprietary compound library and product engine, identifying drug targets and potential product candidates, in-licensing, producing drug substance and drug product material for use in clinical trials and conducting pre-clinical studies and early clinical trials. To date, we have funded our operations primarily through the issuance of convertible notes and convertible preferred stock. Since inception, we have raised an aggregate of \$140.0 million of gross proceeds to fund our operations through the issuance of convertible notes and convertible preferred stock.

We have incurred significant operating losses since our inception and we expect to continue to incur significant operating losses for the foreseeable future. Our ability to generate product revenue sufficient to achieve profitability, if ever, will depend heavily on the successful development and eventual commercialization of one or more of our product candidates. Our net losses were \$23.0 million and \$32.6 million for the years ended December 31, 2017 and 2018, respectively, and \$36.8 million for the three months ended March 31, 2019. As of March 31, 2019, we had an accumulated deficit of \$105.0 million. We expect our expenses and operating losses will increase substantially over the next several years in connection with our ongoing activities, as we:

- continue our clinical development of losmapimod, including our ongoing Phase 1 clinical trial and planned Phase 2b clinical trial and Phase 2 open label clinical trial;
- continue IND-enabling studies and prepare for a planned Phase 1 clinical trial of FTX-HbF;
- advance clinical-stage product candidates into later stage trials;
- pursue the discovery of drug targets for other rare diseases and the subsequent development of any resulting product candidates;

- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- scale up our manufacturing processes and capabilities, or arrange for a third party to do so on our behalf, to support our clinical trials of our product candidates and commercialization of any of our product candidates for which we obtain marketing approval;
- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain regulatory approval;
- acquire or in-license products, product candidates, technologies and/or data referencing rights;
- make any milestone payments to affiliates of GlaxoSmithKline plc, or GSK, under our right of reference and license agreement with GSK upon the achievement of specified clinical or regulatory milestones;
- maintain, expand, enforce, defend and protect our intellectual property;
- hire additional clinical, quality control and scientific personnel; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts and our operations as a public company.

As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through the sale of equity, debt financings or other capital sources, including collaborations with other companies or other strategic transactions. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements as, and when, needed, we may have to significantly delay, scale back or discontinue the development and commercialization of one or more of our product candidates, or grant rights to develop and market our product candidates even if we would otherwise prefer to develop and market such product candidates ourselves.

Because of the numerous risks and uncertainties associated with drug development, we are unable to predict the timing or amount of increased expenses or the timing of when or if we will be able to achieve or maintain profitability. Even if we are able to generate product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

As of March 31, 2019, we had \$62.5 million in cash and cash equivalents. We believe that the anticipated net proceeds from this offering, together with our existing cash and cash equivalents, will enable us to fund our operating expenses and capital expenditure requirements through . We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. See "—Liquidity and Capital Resources."

Without giving effect to the anticipated net proceeds from this offering, based on our current operating plan, we expect that our existing cash and cash equivalents will be sufficient to fund our operating expenses and capital expenditure requirements into the first quarter of 2020. To finance our operations beyond that point we will need to raise additional capital, which cannot be assured. We have concluded that this circumstance raises substantial doubt about our ability to continue as a going concern for at least one year from the date that our consolidated financial statements for the year ended December 31, 2018 and our consolidated financial statements for the three months ended March 31, 2019 were issued. See Note 1 to our annual and interim consolidated financial statements appearing at the end of this prospectus for additional information on our assessment.

Components of Results of Operations

Revenue

We have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products for several years, if at all. If our development efforts for our current or future product candidates are successful and result in marketing approval, we may generate revenue in the future from product sales. We cannot predict if, when or to what extent we will generate revenue from the commercialization and sale of our product candidates. We may never succeed in obtaining regulatory approval for any of our product candidates.

We may also in the future enter into license or collaboration agreements for our product candidates or intellectual property, and we may generate revenue in the future from payments as a result of such license or collaboration agreements.

Operating Expenses

Research and Development Expenses

Research and development expenses represent costs incurred by us for the discovery, development, and manufacture of our product candidates and include:

- external research and development expenses incurred under agreements with contract research organizations, or CROs, contract manufacturing organizations, or CMOs, and consultants;
- salaries, payroll taxes, employee benefits and stock-based compensation expenses for individuals involved in research and development efforts;
- laboratory supplies;
- in-process research and development, or IPR&D, expenses, which relate to IPR&D acquired as part of an asset acquisition for which there is no alternative future use;
- costs related to compliance with regulatory requirements; and
- facilities, depreciation and other allocated expenses, which include direct and allocated expenses for rent, maintenance of facilities, insurance and other operating costs.

We expense research and development costs as incurred. We recognize expenses for certain development activities, such as clinical trials and manufacturing, based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment or other information provided to us by our vendors. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of expenses incurred. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. These amounts are recognized as an expense as the goods are delivered or the related services are performed, or until it is no longer expected that the goods will be delivered or the services rendered.

External costs represent a significant portion of our research and development expenses, which we track on a program-by-program basis following the nomination of a development candidate. Our internal research and development expenses consist primarily of personnel-related expenses, including stock-based compensation expense. We do not track our internal research and development expenses on a program-by-program basis as the resources are deployed across multiple projects.

The following table summarizes our external research and development expenses by program following nomination as a development candidate for the years ended December 31, 2017 and 2018, and for the three months ended March 31, 2018 and 2019. Pre-development candidate expenses, unallocated expenses and internal research and development expenses are classified separately. We nominated

losmapimod as a development candidate in December 2017. FSHD external expenses include IPR&D expenses.

(in thousands)	Year Ended December 31, 2017	Year Ended December 31, 2018	Three Months Ended March 31, 2018	Three Months Ended March 31, 2019
FSHD external expenses	\$ 134	\$ 3,108	\$ 454	\$ 27,802
Pre-development candidate expenses and unallocated expenses	11,143	13,534	3,058	4,029
Internal research and development expenses	7,217	8,542	2,061	2,798
Total research and development expenses	<u>\$ 18,494</u>	<u>\$ 25,184</u>	<u>\$ 5,573</u>	<u>\$ 34,629</u>

The successful development of our product candidates is highly uncertain. At this time, we cannot reasonably estimate or know the nature, timing, and estimated costs of the efforts that will be necessary to complete the remainder of the development of our product candidates. We are also unable to predict when, if ever, material net cash inflows will commence from our product candidates, if approved. This is due to the numerous risks and uncertainties associated with developing our product candidates, including the uncertainty related to:

- the timing and progress of preclinical and clinical development activities;
- the number and scope of preclinical and clinical programs we decide to pursue;
- our ability to raise additional funds necessary to complete clinical development of and commercialize our product candidates;
- our ability to maintain our current research and development programs and to establish new ones;
- our ability to establish new licensing or collaboration arrangements;
- the progress of the development efforts of parties with whom we may enter into collaboration arrangements;
- the successful initiation and completion of clinical trials with safety, tolerability and efficacy profiles that are satisfactory to the U.S. Food and Drug Administration, or FDA, or any comparable foreign regulatory authority;
- the receipt and related terms of regulatory approvals from applicable regulatory authorities;
- the availability of raw materials and active pharmaceutical ingredient, or API, for use in production of our product candidates;
- our ability to establish and operate a manufacturing facility, or secure manufacturing supply through relationships with third parties;
- our ability to consistently manufacture our product candidates in quantities sufficient for use in clinical trials;
- our ability to obtain and maintain intellectual property protection and regulatory exclusivity, both in the United States and internationally;
- our ability to maintain, enforce, defend and protect our rights in our intellectual property portfolio;
- the commercialization of our product candidates, if and when approved;
- our ability to obtain and maintain third-party coverage and adequate reimbursement for our product candidates, if approved;
- the acceptance of our product candidates, if approved, by patients, the medical community and third-party payors;
- competition with other products; and
- a continued acceptable safety profile of our products following receipt of any regulatory approvals.

A change in the outcome of any of these variables with respect to the development of any of our product candidates would significantly change the costs and timing associated with the development of that product candidate, and potentially other candidates.

Research and development activities account for a significant portion of our operating expenses. We expect our research and development expenses to increase significantly in future periods as we continue to implement our business strategy, which includes advancing losmapimod and FTX-HbF through clinical development, expanding our research and development efforts, including hiring additional personnel to support our research and development efforts, and seeking regulatory approvals for our product candidates that successfully complete clinical trials. In addition, product candidates in later stages of clinical development generally incur higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. As a result, we expect our research and development expenses to increase as our product candidates advance into later stages of clinical development. However, we do not believe that it is possible at this time to accurately project total program-specific expenses through commercialization. There are numerous factors associated with the successful commercialization of any of our product candidates, including future trial design and various regulatory requirements, many of which cannot be determined with accuracy at this time based on our stage of development.

General and Administrative Expenses

General and administrative expenses consist of personnel-related costs, including salaries, benefits and stock-based compensation expense, for our personnel in executive, finance and accounting, human resources, business operations and other administrative functions, legal fees related to patent, intellectual property and corporate matters, fees paid for accounting and tax services, consulting fees and facility-related costs not otherwise included in research and development expenses.

We expect our general and administrative expenses will increase for the foreseeable future to support our expanded infrastructure and increased costs of expanding our operations and operating as a public company. These increases will likely include increased expenses related to accounting, audit, legal, regulatory and tax-related services associated with maintaining compliance with exchange listing and SEC requirements, director and officer insurance premiums, and investor relations costs associated with operating as a public company.

Other Income, Net

Other income, net consists primarily of interest income related to our investments in cash equivalents and proceeds from the sale of drug material to a third party during February 2018.

Results of Operations**Comparison of the Three Months Ended March 31, 2018 and 2019**

The following summarizes our results of operations for the three months ended March 31, 2018 and 2019, along with the changes in those items in dollars:

<u>(in thousands)</u>	<u>Three Months Ended</u>		<u>Change</u>
	<u>March 31,</u>		
	<u>2018</u>	<u>2019</u>	<u>\$</u>
Operating expenses:			
Research and development	\$ 5,573	\$ 34,629	\$ 29,056
General and administrative	1,737	2,598	861
Total operating expenses	7,310	37,227	29,917
Loss from operations	(7,310)	(37,227)	(29,917)
Other income, net	370	384	14
Net loss	\$ (6,940)	\$ (36,843)	\$ (29,903)

Research and Development Expenses

Research and development expense increased by \$29.0 million from \$5.6 million for the three months ended March 31, 2018 to \$34.6 million for the three months ended March 31, 2019. The increase in research and development expense was primarily attributable to the following:

- \$25.6 million in increased IPR&D expenses associated with the recognition of the fair value attributable to the right of reference and license agreement with GSK during the three months ended March 31, 2019;
- \$1.8 million in increased costs for external clinical activities as we advanced losmapimod into a Phase 1 clinical trial and conducted preparatory studies in anticipation of initiating Phase 2 clinical trials in mid-2019;
- \$0.8 million in increased personnel-related costs due to increased headcount, including \$0.2 million of increased stock-based compensation expense; and
- \$0.3 million in increased laboratory supplies to support our expanding research efforts.

General and Administrative Expenses

General and administrative expenses increased by \$0.9 million from \$1.7 million for the three months ended March 31, 2018 to \$2.6 million for the three months ended March 31, 2019. The increase in general and administrative expenses was primarily attributable to the following:

- \$0.6 million in increased personnel-related costs, primarily due to increased general and administrative headcount to support the growth of our research and development organization, including \$0.2 million of increased stock-based compensation expense; and
- \$0.2 million in increased consulting and professional fees, including for legal services, market research, recruiting, accounting, and tax.

Other Income, Net

Other income, net increased by less than \$0.1 million from \$0.4 million for the three months ended March 31, 2018 to \$0.4 million for the three months ended March 31, 2019. Other income, net during the three months ended March 31, 2019 was primarily attributable to investment income of \$0.4 million from cash equivalents. During the three months ended March 31, 2018, other income, net related primarily to the sale of drug material to a third party for \$0.4 million.

Comparison of the Years Ended December 31, 2017 and 2018

The following summarizes our results of operations for the years ended December 31, 2017 and 2018, along with the changes in those items in dollars:

(in thousands)	Year Ended December 31,		Change
	2017	2018	\$
Operating expenses:			
Research and development	\$ 18,494	\$ 25,184	\$ 6,690
General and administrative	4,499	8,314	3,815
Total operating expenses	22,993	33,498	10,505
Loss from operations	(22,993)	(33,498)	(10,505)
Other income, net	29	910	881
Net loss	\$ (22,964)	\$ (32,588)	\$ (9,624)

Research and Development Expenses

Research and development expense increased by \$6.7 million from \$18.5 million for the year ended December 31, 2017 to \$25.2 million for the year ended December 31, 2018. The increase in research and development expense was primarily attributable to the following:

- \$2.4 million in increased facility-related costs, including rent and other costs related to our new facility lease that commenced in December 2017, depreciation and other utility and maintenance costs;
- \$1.6 million in increased external manufacturing costs related to losmapimod and increased chemistry efforts for our hemoglobinopathies program;
- \$1.3 million in increased personnel-related costs due to increased headcount, including \$0.3 million of increased stock-based compensation expense;
- \$0.9 million in increased costs for preparatory studies in anticipation of initiating losmapimod clinical trials in 2019; and
- \$0.4 million in increased laboratory supplies to support our expanding research efforts.

General and Administrative Expenses

General and administrative expenses increased by \$3.8 million from \$4.5 million for the year ended December 31, 2017 to \$8.3 million for the year ended December 31, 2018. The increase in general and administrative expenses was primarily attributable to the following:

- \$1.9 million in increased personnel-related costs, primarily due to increased general and administrative headcount to support the growth of our research and development organization, including \$0.5 million of increased stock-based compensation expense;
- \$1.1 million in increased consulting and professional fees, including for legal services, market research, recruiting, accounting and tax; and
- \$0.4 million in increased facility-related costs, including rent and other costs related to our new facility lease that commenced in December 2017, depreciation and other utility and maintenance costs.

Other Income, Net

Other income, net increased by \$0.9 million from less than \$0.1 million for the year ended December 31, 2017 to \$0.9 million for the year ended December 31, 2018. The increase in other income, net was primarily attributable to an increase in investment income of \$0.5 million during the year ended

December 31, 2018 due to higher cash equivalents in 2018 and the sale of drug material to a third party in February 2018 for \$0.4 million.

Liquidity and Capital Resources

Sources of Liquidity

We have incurred significant operating losses since our inception and expect to continue to incur significant operating losses for the foreseeable future and may never become profitable. We have not yet commercialized any of our product candidates, which are in various phases of preclinical and clinical development, and we do not expect to generate revenue from sales of any products for several years, if at all. We have primarily funded our operations through March 31, 2019 with aggregate gross proceeds of \$140.0 million from the issuance of convertible notes and convertible preferred stock. As of March 31, 2019, we had cash and cash equivalents of \$62.5 million.

Cash Flows

The following table provides information regarding our cash flows for the years ended December 31, 2017 and 2018, and for the three months ended March 31, 2018 and 2019:

(in thousands)	Year Ended December 31, 2017	Year Ended December 31, 2018	Three Months Ended March 31, 2018	Three Months Ended March 31, 2019
Net cash used in operating activities	\$ (20,074)	\$ (22,562)	\$ (6,632)	\$ (9,897)
Net cash used in investing activities	(1,908)	(8,981)	(783)	(401)
Net cash provided by (used in) financing activities	17,662	105,025	12,640	(47)
Net (decrease) increase in cash, cash equivalents, and restricted cash	<u>\$ (4,320)</u>	<u>\$ 73,482</u>	<u>\$ 5,225</u>	<u>\$ (10,345)</u>

Net Cash Used in Operating Activities

Net cash used in operating activities was \$9.9 million during the three months ended March 31, 2019 compared to net cash used in operating activities of \$6.6 million during the three months ended March 31, 2018. The increase in net cash used in operating activities of \$3.3 million was due to an increase in net loss of \$29.9 million for the three months ended March 31, 2019 as compared to the three months ended March 31, 2018, partially offset by a net increase in non-cash expenses of \$26.3 million primarily due to an increase in IPR&D expenses of \$25.6 million and an increase in stock-based compensation expense of \$0.4 million, and a net increase in cash provided by changes in our operating assets and liabilities of \$0.3 million.

Net cash used in operating activities was \$22.6 million during the year ended December 31, 2018 compared to net cash used in operating activities of \$20.1 million during the year ended December 31, 2017. The increase in net cash used in operating activities of \$2.5 million was due to an increase in net loss of \$9.6 million for the year ended December 31, 2018 as compared to the year ended December 31, 2017, partially offset by a net increase in cash provided by changes in our operating assets and liabilities of \$5.7 million, primarily due to the receipt of \$4.6 million during the year ended December 31, 2018 associated with the leasehold improvement allowance related to our new facility lease that commenced in December 2017, and a net increase in non-cash expenses of \$1.4 million.

Net Cash Used in Investing Activities

Net cash used in investing activities was \$0.4 million during the three months ended March 31, 2019 compared to net cash used in investing activities of \$0.8 million during the three months ended March 31, 2018. Net cash used in investing activities for the three months ended March 31, 2019 and 2018 primarily consisted of purchases of property and equipment.

Net cash used in investing activities was \$9.0 million during the year ended December 31, 2018 compared to net cash used in investing activities of \$1.9 million during the year ended December 31, 2017. Net cash used in investing activities for the years ended December 31, 2018 and 2017 consisted of purchases of property and equipment. The increase in net cash used in investing activities of \$7.1 million was primarily due to an increase in purchases of property and equipment associated with our new facility lease that commenced in December 2017.

Net Cash Provided by (Used in) Financing Activities

Net cash used in financing activities was less than \$0.1 million during the three months ended March 31, 2019 compared to net cash provided by financing activities of \$12.6 million during the three months ended March 31, 2018. The cash provided by financing activities during the three months ended March 31, 2018 was primarily the result of \$12.7 million of net proceeds received from private placements of our Series A preferred stock. The net cash used in financing activities for the three months ended March 31, 2019 was primarily the result of the payment of costs associated with the issuance of Series B preferred stock.

Net cash provided by financing activities was \$105.0 million during the year ended December 31, 2018 compared to \$17.7 million during the year ended December 31, 2017. The cash provided by financing activities during the year ended December 31, 2018 was primarily the result of \$105.1 million of net proceeds received from private placements of our Series A and Series B preferred stock. The cash provided by financing activities for the year ended December 31, 2017 was primarily the result of \$17.6 million of net proceeds received from private placements of our Series A preferred stock.

Funding Requirements

We expect our expenses to increase substantially in connection with our ongoing research and development activities, particularly as we continue the research and development of, initiate clinical trials of, and seek marketing approval for, our product candidates. In addition, upon the closing of this offering, we expect to incur additional costs associated with operating as a public company. As a result, we expect to incur substantial operating losses and negative operating cash flows for the foreseeable future.

Based on our current operating plan, we expect that the anticipated net proceeds from this offering, together with our existing cash and cash equivalents, will enable us to fund our operating expenses and capital expenditure requirements through . However, we have based this estimate on assumptions that may prove to be wrong and we could exhaust our capital resources sooner than we expect.

Our funding requirements and timing and amount of our operating expenditures will depend largely on:

- the progress, costs and results of our ongoing Phase 1 clinical trial of losmapimod;
- the scope, progress, results and costs of discovery research, preclinical development, laboratory testing and clinical trials for our product candidates, including our planned Phase 2b clinical trial and planned Phase 2 open label clinical trial of losmapimod and our planned Phase 1 clinical trial of FTX-HbF;
- the number of and development requirements for other product candidates that we pursue;
- the costs, timing and outcome of regulatory review of our product candidates;
- our ability to enter into contract manufacturing arrangements for supply of API and manufacture of our product candidates and the terms of such arrangements;
- our ability to establish and maintain strategic collaborations, licensing or other arrangements and the financial terms of such arrangements;
- the payment or receipt of milestones and receipt of other collaboration-based revenues, if any;

- the costs and timing of future commercialization activities, including product manufacturing, sales, marketing and distribution, for any of our product candidates for which we may receive marketing approval;
- the amount and timing of revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property and proprietary rights and defending any intellectual property-related claims; and
- the extent to which we acquire or in-license other products, product candidates, technologies or data referencing rights.

A change in the outcome of any of these or other variables with respect to the development of any of our product candidates could significantly change the costs and timing associated with the development of that product candidate. We will need to continue to rely on additional financing to achieve our business objectives.

In addition to the variables described above, if and when any of our product candidates successfully complete development, we will incur substantial additional costs associated with regulatory filings, marketing approval, post-marketing requirements, maintaining our intellectual property rights, and regulatory protection, in addition to other commercial costs. We cannot reasonably estimate these costs at this time.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity or debt financings and collaboration arrangements. We currently have no credit facility or committed sources of capital. To the extent that we raise additional capital through the future sale of equity securities, the ownership interests of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing common stockholders. If we raise additional funds through the issuance of debt securities, these securities could contain covenants that would restrict our operations. We may require additional capital beyond our currently anticipated amounts, and additional capital may not be available on reasonable terms, or at all. If we raise additional funds through collaboration arrangements or other strategic transactions in the future, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates, or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations

The following table summarizes our contractual obligations as of December 31, 2018 and the effects that these obligations are expected to have on our liquidity and cash flows in future periods:

(in thousands)	Total	Less Than 1 Year	1 to 3 Years	3 to 5 Years	More Than 5 Years
Operating lease commitments ⁽¹⁾	\$ 23,966	\$ 2,219	\$ 4,639	\$ 4,921	\$ 12,187
Capital lease obligation	124	53	71	—	—
	<u>\$ 24,090</u>	<u>\$ 2,272</u>	<u>\$ 4,710</u>	<u>\$ 4,921</u>	<u>\$ 12,187</u>

(1) Represents future minimum lease payments under our non-cancelable operating lease, which expires in June 2028. The minimum lease payments above do not include any related common area maintenance charges or real estate taxes.

Under our right of reference and license agreement that we entered into in February 2019 with affiliates of GSK, we have payment obligations that are contingent upon the occurrence of future events

such as our achievement of specified clinical, regulatory and sales milestones and are required to make royalty payments in connection with the sale of products developed under the agreement. Specifically, we may owe GSK up to \$37.5 million in certain specified clinical and regulatory milestones, of which \$2.5 million is due upon the initiation of a Phase 2 clinical trial, and up to \$60.0 million in certain specified sales milestones and royalties on product sales, if any. We have not included any such contingent milestone or royalty payment obligations in the table above, which is presented as of December 31, 2018. In addition, the amount (in the case of potential royalty payments), timing and likelihood of such payments are not always known. For additional information regarding this license agreement, including our payment obligations thereunder, see "Business—Right of Reference and License Agreement with GlaxoSmithKline," Note 14 to our annual consolidated financial statements included elsewhere in this prospectus and Note 9 to our interim consolidated financial statements included elsewhere in this prospectus.

We enter into contracts in the normal course of business with CROs, CMOs and other third parties for clinical trials, pre-clinical research studies, synthetic chemistry and testing and manufacturing services. These contracts are generally cancelable by us upon up to 30 days' prior written notice. Payments due upon cancellation consist only of payments for services provided or expenses incurred, including noncancelable obligations of our service providers, up to and through the date of cancellation. These payments are not included in the preceding table as the amount and timing of these payments are not known.

Off-Balance Sheet Arrangements

We did not have, during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined in the rules and regulations of the SEC.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these consolidated financial statements requires us to make judgments and estimates that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, and the reported amounts of expenses during the reported periods. Our estimates are based on our historical experience, known trends and events, and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities and amount of expense recognized that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. We evaluate our estimates and assumptions on an ongoing basis. The effects of material revisions in estimates, if any, will be reflected in the consolidated financial statements prospectively from the date of change in estimates.

We believe that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the most significant areas involving management's judgments and estimates. See Note 2 to our annual consolidated financial statements included elsewhere in this prospectus for a description of our other significant accounting policies.

Accrued Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued expenses as of each balance sheet date. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers

and make adjustments if necessary. The significant estimates in our accrued research and development expenses include the costs incurred for services performed by our vendors in connection with research and development activities for which we have not yet been invoiced.

We base our expenses related to research and development activities on our estimates of the services received and efforts expended pursuant to quotes and contracts with vendors that conduct research and development on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the research and development expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid expense accordingly. Non-refundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts actually incurred.

Stock-Based Compensation

We measure stock-based compensation expense related to all restricted stock awards and stock options based on the fair value of the award on the date of grant. We recognize compensation expense for these awards over the requisite service period, which is generally the vesting period of the respective award. Generally, we issue awards with only service-based vesting conditions and record the expense for these awards using the straight-line method. We have also granted certain stock-based awards with performance-based vesting conditions. We recognize compensation expense for awards with performance-based vesting conditions over the remaining service period using an accelerated attribution method when management determines that achievement of the performance condition is probable. At each reporting date, we evaluate if the achievement of a performance-based milestone is probable based on the expected satisfaction of the performance conditions.

We determine the fair value of restricted stock awards based on the estimated fair value of our common stock on the date of grant, less any applicable purchase price. We estimate the fair value of stock options granted using the Black-Scholes option-pricing model. The determination of the grant date fair value of stock options using an option pricing model is affected principally by our estimated fair value of our common stock and requires management to make a number of other assumptions, including the expected term of the option, the estimated volatility of the underlying shares, the risk-free interest rate, and expected dividends. The assumptions used in the determination of the grant date fair value of stock options represent management's best estimates at the time of measurement. As a result of the lack of a public market for the trading of our common stock and a lack of company-specific historical and implied volatility data, we base the estimate of expected volatility on the historical volatility of a representative group of publicly traded companies for which historical information is available. The historical volatility is calculated based on a period of time commensurate with the assumption used for the expected term. We use the simplified method to calculate the expected term for all stock options. We utilize this method as we do not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. The risk-free interest rate is based on a U.S. treasury instrument whose term is consistent with the expected term of the stock options. The expected dividend yield is assumed to be zero as we have never paid dividends and do not have current plans to pay any dividends on common stock.

In future periods, we expect stock-based compensation expense to increase, due in part to our existing unrecognized stock-based compensation expense and as we grant additional stock-based awards to continue to attract and retain our employees.

Fair Value of Common Stock and Series B Preferred Stock

As previously described, we are required to estimate the fair value of our common stock underlying our stock-based awards when estimating the grant date fair value of those awards. Additionally, we were required to estimate the fair value of the Series B preferred stock issued pursuant to the right of reference and license agreement that we entered into with GSK in February 2019. As there has been no public market for our common stock or Series B preferred stock to date, the estimated fair value of our common stock and Series B preferred stock has been determined by our board of directors and management, respectively, as of the date of each equity issuance considering our most recently available third-party valuations of common stock or Series B preferred stock, and our assessment of additional objective and subjective factors. These third-party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, Valuation of Privately-Held-Company Equity Securities Issued as Compensation. Our common stock valuations were prepared using the guideline public company method and/or the precedent transaction method to estimate our equity value, and we utilized the option-pricing method, or OPM, or the hybrid method to allocate equity value to our common stock and preferred stock. The hybrid method is a probability-weighted expected return method, or PWERM, where the equity value in one or more of the scenarios is allocated using an OPM. The OPM treats common stock and preferred stock as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. Under this method, the common stock has value only if the funds available for distribution to stockholders exceeded the value of the preferred stock liquidation preferences at the time of the liquidity event, such as a strategic sale or a merger or an initial public offering, or IPO. The PWERM is a scenario-based method that estimates the fair value of common stock and preferred stock based upon an analysis of future values for the company, assuming various outcomes. The common stock and preferred stock value is based on the probability-weighted present value of expected future investment returns considering each of the possible outcomes available, as well as the rights of each class of stock. The future value of the common stock and preferred stock under each outcome is discounted back to the valuation date at an appropriate risk-adjusted discount rate and probability weighted to arrive at an indication of value for the common stock. In our application of the hybrid method, we considered an IPO scenario under the PWERM framework, in which the shares of convertible preferred stock are assumed to convert to common stock, and a non-IPO scenario modeled using an OPM. Our Series B preferred stock valuation was prepared using the hybrid method. The relative probability of the IPO scenario was determined based on an analysis of market conditions at the time and our expectations as to the timing and likely prospects of the IPO at each valuation date. In our application of the guideline public company method, we considered recently completed IPOs as indicators of our estimated future value in an IPO.

Based on our early stage of development and other relevant factors, our board of directors determined that the OPM was the most appropriate method for allocating our enterprise value to determine the estimated fair value of our common stock for the valuations performed as of December 31, 2016, December 31, 2017 and June 1, 2018, which resulted in our board of directors determining that the fair value of our common stock was \$0.42 per share, \$0.47 per share and \$0.69 per share, respectively. Following the issuance of the Series B preferred stock in August 2018, our board of directors determined that the hybrid method was the most appropriate method for allocating our enterprise value to determine the estimated fair value of our common stock for valuations performed as of August 24, 2018, November 30, 2018, March 15, 2019 and May 10, 2019, which resulted in our board of directors determining that the fair value of our common stock was \$1.09 per share, \$1.12 per share, \$1.19 per share and \$1.58 per share, respectively. Our board of directors determined that it was appropriate to change the methodology for determining the fair value of our common stock to the hybrid method beginning with the

August 24, 2018 valuation as greater certainty developed regarding a possible IPO upon the issuance of the Series B preferred stock. Management determined that the value of our Series B preferred stock was \$2.04 per share as of February 8, 2019.

Our board of directors and management considered various objective and subjective factors to determine the fair value of our common stock and Series B preferred stock, respectively, including:

- valuations of our common stock and Series B preferred stock performed by independent third-party valuation specialists;
- our stage of development and business strategy, including the status of research and development efforts of our product candidates;
- the analysis of IPOs and the valuation of similar publicly traded companies in the biopharmaceutical industry;
- our financial position, including our levels of available capital resources;
- the lack of an active public market for our common stock and our preferred stock;
- the prices of our convertible preferred stock sold to investors in arm's length transactions and the rights, preferences and privileges of our convertible preferred stock relative to those of our common stock;
- the likelihood and potential timing of achieving a liquidity event, such as an IPO, in light of prevailing market conditions; and
- external market conditions affecting the biotechnology industry, and trends within the biopharmaceutical industry.

The assumptions underlying these valuations represent our best estimates, which involve inherent uncertainties and the application of judgment. As a result, if factors or expected outcomes change and we use significantly different assumptions or estimates, our stock-based compensation expense or in-process research and development expense could be materially different.

Once a public trading market for our common stock has been established in connection with the completion of this offering, it will no longer be necessary for our board of directors to estimate the fair value of our common stock in connection with our accounting for granted stock options and other such awards we may grant, as the fair value of our common stock will be determined based on the quoted market price of our common stock.

Grants of Stock-Based Awards

The following table presents the grant dates, numbers of underlying shares of common stock, the per share purchase prices and exercise prices, and the fair values of the underlying common stock as of the grant dates for awards granted between January 1, 2018 and May 31, 2019, along with the fair value per award on the date of grant:

Grant Date	Type of Award	Number of Shares Subject to Awards Granted	Per Share Exercise Price or Purchase Price	Per Share Fair Value of Common Stock on Grant Date	Per Share Estimated Fair Value of Award on Grant Date ⁽¹⁾
1/23/2018	Restricted Stock	1,580,013	\$ 0.01	\$ 0.47(2)	\$ 0.46
2/23/2018	Restricted Stock	170,000	\$ 0.01	\$ 0.47(2)	\$ 0.46
6/20/2018	Restricted Stock	47,000	\$ 0.01	\$ 0.69	\$ 0.68
6/20/2018	Stock Options	578,932	\$ 0.69	\$ 0.69	\$ 0.49
7/11/2018	Stock Options	240,500	\$ 0.69	\$ 0.69	\$ 0.50
10/17/2018	Stock Options	502,370	\$ 1.09	\$ 1.09	\$ 0.77
12/13/2018	Stock Options	108,500	\$ 1.12	\$ 1.12	\$ 0.79
12/18/2018	Stock Options	2,125,000	\$ 1.12	\$ 1.12	\$ 0.79
1/22/2019	Stock Options	7,043,661	\$ 1.12	\$ 1.12	\$ 0.79
3/20/2019	Stock Options	100,000	\$ 1.19	\$ 1.19	\$ 0.84
5/21/2019	Stock Options	658,000	\$ 1.58	\$ 1.58	\$ 1.11

- (1) For restricted stock, the Per Share Estimated Fair Value of Award on Grant Date reflects the weighted average fair value of restricted stock at the date of grant, which is equal to the fair value of our common stock as of the date of grant as determined by our board of directors, less the applicable purchase price of the restricted stock. For stock options, the Per Share Estimated Fair Value of Award on Grant Date reflects the weighted average fair value of stock options as estimated at the date of grant using the Black-Scholes option-pricing model.
- (2) We undertook a retrospective valuation of the fair value of our common stock as of December 31, 2017 and this value represents our estimated fair value per common share in accordance with such retrospective valuation.

Stock Option Grants in Connection with Initial Public Offering

Our board of directors has approved, effective upon the commencement of trading of our common stock on the Nasdaq Stock Market, grants of stock options to purchase an aggregate of 2,159,544 shares of our common stock at a purchase price per share equal to the estimated fair market value of our common stock on such date of grant, which our board of directors determined to be equal to the initial public offering price of our common stock in this offering.

Income Taxes

We account for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the consolidated financial statements or in our tax returns. Under this method, deferred tax assets and liabilities are determined based on differences between the financial statement carrying amounts and the tax bases of the assets and liabilities using the enacted tax rates in effect in the years in which the differences are expected to reverse. A valuation allowance against deferred tax assets is recorded if, based on the weight of the available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. Potential for recovery of deferred tax assets is evaluated by considering several factors, including estimating the future taxable profits expected, estimating future reversals of existing taxable temporary differences, considering taxable profits in carryback periods, and considering prudent and feasible tax planning strategies.

We account for uncertain tax positions using a more-likely-than-not threshold for recognizing and resolving uncertain tax positions. The evaluation of uncertain tax positions is based on factors including, but not limited to, changes in the law, the measurement of tax positions taken or expected to be taken in tax returns, the effective settlement of matters subject to audit, new audit activity, and changes in facts or circumstances related to a tax position. As of each balance sheet date, we did not have any uncertain tax positions.

Recently Issued Accounting Pronouncements

We have reviewed all recently issued standards and have determined that, other than as disclosed in Note 2 to our annual and interim consolidated financial statements appearing at the end of this prospectus, these standards will not have a material impact on our financial statements or do not otherwise apply to our operations.

Quantitative and Qualitative Disclosures about Market Risk

Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our cash equivalents are in the form of money market funds that are invested in U.S. Treasury securities. As of March 31, 2019, we had cash and cash equivalents of \$62.5 million. Interest income is sensitive to changes in the general level of interest rates; however, due to the nature of these investments, an immediate 10% change in interest rates would not have a material effect on the fair market value of our investment portfolio.

We are also exposed to market risk related to changes in foreign currency exchange rates. We contract with vendors that are located outside of the United States and certain invoices are denominated in foreign currencies. We are subject to fluctuations in foreign currency rates in connection with these arrangements. We do not currently hedge our foreign currency exchange rate risk. As of March 31, 2019, we had minimal or no liabilities denominated in foreign currencies.

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation had a material effect on our business, financial condition or results of operations during the years ended December 31, 2017 and 2018 or the three months ended March 31, 2018 and 2019.

Emerging Growth Company Status

As an emerging growth company, or EGC, under the Jumpstart Our Business Startups Act of 2012, or JOBS Act, we may delay the adoption of certain accounting standards until such time as those standards apply to private companies. Other exemptions and reduced reporting requirements under the JOBS Act for EGCs include presentation of only two years of audited financial statements in a registration statement for an IPO, an exemption from the requirement to provide an auditor's report on internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act of 2002, an exemption from any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation, and less extensive disclosure about our executive compensation arrangements. Additionally, the JOBS Act provides that an EGC can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an EGC to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to avail ourselves of this exemption and, therefore, while we are an EGC, we will not be subject to new or revised accounting standards at the same time that they become applicable to other public companies that are not EGCs. As a result, our consolidated financial statements may not be comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates.

We may remain classified as an EGC until the end of the fiscal year in which the fifth anniversary of this offering occurs, although if the market value of our common stock that is held by non-affiliates exceeds \$700 million as of any June 30 before that time or if we have annual gross revenues of \$1.07 billion or more in any fiscal year, we would cease to be an EGC as of December 31 of the applicable year. We also would cease to be an EGC if we issue more than \$1 billion of non-convertible debt over a three-year period.

BUSINESS

Overview

We are a clinical-stage biopharmaceutical company focused on improving the lives of patients with genetically defined diseases in areas of high unmet medical need, with an initial focus on rare diseases. We have developed a proprietary product engine that we employ to systematically identify and validate cellular drug targets that can potentially modulate gene expression to treat the known root cause of genetically defined diseases. We are using our product engine to identify targets that can be drugged by small molecules regardless of the particular underlying mechanism of gene mis-expression. We have identified drug targets to treat the root causes of facioscapulohumeral muscular dystrophy, or FSHD, and certain hemoglobinopathies, namely sickle cell disease, or SCD, and β -thalassemia. We expect to initiate a Phase 2b clinical trial of losmapimod, our product candidate for FSHD, in mid-2019. We commenced a Phase 1 clinical trial in February 2019 to obtain safety and tolerability data for losmapimod in patients with FSHD. We plan to submit an investigational new drug application, or IND, for FTX-HbF, our product candidate for certain hemoglobinopathies, in mid-2020.

We are using our proprietary product engine to identify and validate drug targets and develop product candidates to address diseases caused by the mis-expression of certain genes. Our product engine integrates patient-derived tissue-relevant cell models and drug target screens with our pharmacologically-diverse small molecule compound library and customized CRISPR libraries. We also employ computational biology and FulcrumSeek, our proprietary relational database, to guide target selection and to generate hypotheses on other targets that might be relevant along a gene regulatory pathway.

Our first product candidate, losmapimod, is a small molecule that we are developing for the treatment of FSHD, a rare, progressive and disabling muscle wasting disorder that leads to significant physical impairments and disability. Losmapimod selectively targets p38a/b mitogen activated protein kinase, or p38a/b. We utilized our product engine to discover that inhibition of p38a/b reduced expression of the *DUX4* gene in muscle cells derived from patients with FSHD. The mis-expression of the *DUX4* gene is the known root cause of FSHD. There are no approved therapies for FSHD, one of the most common forms of muscular dystrophy, with an estimated patient population of 16,000 to 38,000 in the United States.

Following our discovery of the role of p38a/b inhibitors in the reduction of *DUX4* expression, we performed an extensive review of known compounds. As a result of our evaluation, we identified losmapimod as the preferred developmental candidate based on the substantial and attractive preclinical and clinical data. We in-licensed losmapimod from affiliates of GlaxoSmithKline, or GSK, in February 2019. GSK had previously treated nearly 3,500 subjects with losmapimod across multiple clinical trials, including one Phase 3 clinical trial. GSK did not conduct a clinical trial of losmapimod in patients with FSHD or any other muscle disorder. We have conducted extensive preclinical testing of losmapimod in patient-derived tissue-relevant cell models and have observed that losmapimod selectively reduced *DUX4*-driven gene expression and restored a healthy gene expression signature with minimal impact on healthy human muscle cells or other cell types.

We plan to conduct a randomized, double-blind placebo-controlled Phase 2b clinical trial to investigate whether treatment with losmapimod reduces *DUX4*-driven gene expression in affected skeletal muscle. In this Phase 2b clinical trial, we will also evaluate the safety and tolerability of losmapimod. We plan to concurrently conduct an open label Phase 2 clinical trial to investigate the safety and tolerability of chronic treatment with losmapimod in patients with FSHD. In this open label trial, we will also evaluate the ability of losmapimod to reduce *DUX4*-driven gene expression in affected skeletal muscle over varying treatment durations. We expect to initiate the Phase 2b clinical trial at multiple sites in the United States and Europe and the open label Phase 2 clinical trial in Europe in mid-2019. We expect to complete a Phase 1 clinical trial in healthy volunteers and patients with FSHD in 2019. We utilized data from GSK's clinical trials of losmapimod and our preclinical data to submit in May 2019 an IND, and clinical trial applications, or CTAs, in Europe and Canada, that will enable us to advance our clinical development plan

for losmapimod in FSHD, including initiating a Phase 2b clinical trial in mid-2019. The FDA accepted the IND in June 2019. The timing of the initiation of the Phase 2b clinical trial is not dependent on the completion of the Phase 1 clinical trial.

We are additionally conducting several preparatory studies to assess biomarker endpoints and clinical outcome assessments and are participating in a natural history study that will follow 150 subjects with FSHD in the United States and 70 subjects in Europe over 18 months. We expect to utilize the data generated from our preparatory studies and the natural history study to inform future clinical trial designs and discussions with regulatory agencies. We believe that these preparatory studies and the safety data from GSK's prior losmapimod clinical trials, together with safety and efficacy data generated from our Phase 1 and Phase 2 clinical trials, may enable us to apply for accelerated approval of losmapimod for the treatment of FSHD. If we observe positive results in our Phase 2b clinical trial based on our proposed biomarker efficacy endpoint of measuring DUX4-driven gene expression in muscle biopsies, we plan to discuss accelerated approval with regulatory agencies and may seek accelerated approval if such regulatory agencies agree that our biomarker endpoint is sufficiently predictive of clinical benefit. The FDA or other regulatory authorities may require us to conduct comparability assessments of GSK-manufactured tablets to tablets manufactured by us or another party.

Our second product candidate, FTX-HbF, is a small molecule designed to upregulate fetal hemoglobin in patients with SCD and b-thalassemia. SCD is a genetic blood disorder caused by a mutation in the b-subunit gene, or *HBB* gene. This mutation results in the formation of abnormal hemoglobin, which causes red blood cells, or RBCs, to change from a round shape into a sickle shape that significantly impairs their function. b-thalassemia is a rare blood disorder caused by various genetic mutations in the *HBB* gene that can significantly impair the production of RBCs.

We designed FTX-HbF to compensate for the root cause of these hemoglobinopathies by inducing the expression of the two g-globin genes, *HBG1/2*, whose expression is normally silenced shortly after birth. The *HBG1/2* genes encode for g-globin, a component of fetal hemoglobin, which is known to compensate for the presence of abnormal hemoglobin in SCD and b-thalassemia. We have observed *in vitro* and *in vivo* activation of the *HBG1/2* genes in preclinical studies with FTX-HbF. We have also observed that FTX-HbF demonstrated robust levels of fetal hemoglobin elevation with no adverse effect on important cellular health markers. We have initiated IND-enabling studies and plan to submit an IND for FTX-HbF in mid-2020.

According to the National Institutes of Health, or NIH, there are approximately 7,000 rare, genetically defined human diseases, many of which have inadequate or no approved treatments. We plan to utilize our product engine to complete four new drug target identification screens in 2019 in Duchenne muscular dystrophy, Friedreich ataxia, myotonic dystrophy 1 and a-synucleinopathies. We also expect to complete an additional six screens in 2020. Our current drug target identification and development efforts are focused on rare neuromuscular disorders, hemoglobinopathies and central nervous system, or CNS, diseases. We also anticipate utilizing our product engine to discover drug targets for genetically defined diseases in other therapeutic areas. In addition to drug targets that we prioritize for internal development, we may identify other drug targets that we would consider for development through partnerships.

Our Pipeline

We designed our proprietary product engine with potential application across a broad array of genetically defined diseases with a known root cause. The following chart summarizes key information about our lead product candidates.

PROGRAM (PRODUCT CANDIDATE)	DIRECTION OF GENE MODULATION	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	NEXT MILESTONE
FSHD (losmapimod)	DUX4 ↓	[Progress bar from Discovery to Phase 1]					Initiate Phase 2b trial in mid-2019 Complete enrollment in Phase 1 trial in mid-2019
Sickle Cell Disease (FTX-HbF)	HBG 1/2 ↑	[Progress bar from Discovery to Preclinical]					Submit IND in mid-2020
β-Thalassemia (FTX-HbF)	HBG 1/2 ↑	[Progress bar from Discovery to Preclinical]					Submit IND in mid-2020

The following chart summarizes key information about our discovery stage pipeline:

DISCOVERY SCREENING INDICATIONS	DIRECTION OF GENE MODULATION	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	STATUS
Duchenne Muscular Dystrophy	UTRN ↑	[Progress bar from Discovery to Preclinical]					Target ID / Validation
Friedreich Ataxia	FXN ↑	[Progress bar from Discovery to Preclinical]					Target ID / Validation
Myotonic Dystrophy 1	DMPK ↓	[Progress bar from Discovery to Preclinical]					Target ID / Validation
α-Synucleinopathies	SCNA ↓	[Progress bar from Discovery to Preclinical]					Target ID / Validation

Our Strategy

We are leveraging the broad applicability of our proprietary product engine to discover and develop small molecule therapies that modulate gene expression to address the known root cause of genetically defined diseases in areas of high unmet medical need, with an initial focus on rare diseases. We believe that our initial product candidates for the treatment of FSHD, SCD and b-thalassemia may have the potential to treat patients with these debilitating and, in some cases, life-threatening illnesses. The key components of our strategy include:

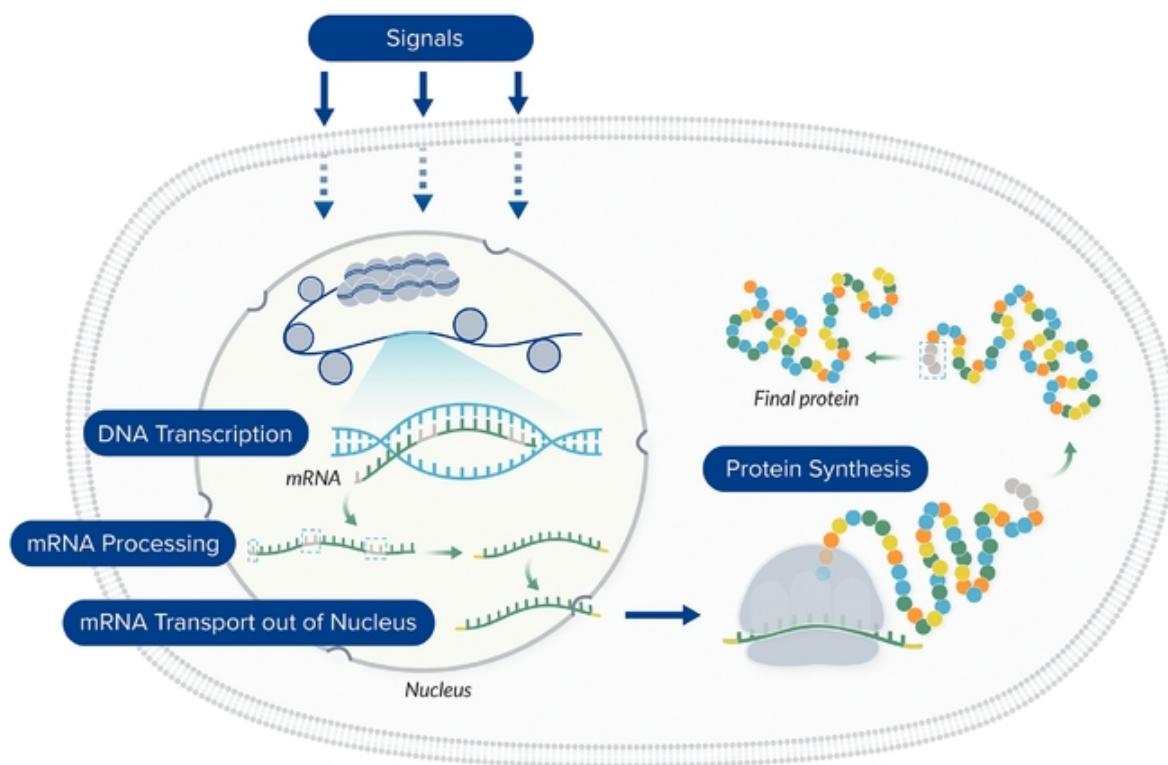
- **Rapidly develop losmapimod for the treatment of FSHD.** We aim to rapidly develop losmapimod for the treatment of FSHD through clinical development and regulatory approval. We plan to initiate a Phase 2b clinical trial of losmapimod in mid-2019 and, subject to positive results, plan to meet with regulators to discuss the potential to pursue accelerated approval given the significant unmet medical need in FSHD and the absence of approved therapies for patients.
- **Advance FTX-HbF into clinical development.** We have initiated IND-enabling studies of FTX-HbF and we aim to submit an IND in mid-2020. We intend to develop FTX-HbF for the treatment of SCD and certain types of b-thalassemia.
- **Continue to apply our proprietary product engine to grow our portfolio of product candidates for the treatment of genetically defined diseases.** We have developed a rigorous assessment and selection process to determine which of the approximately 7,000 rare, genetically defined diseases we intend to evaluate in drug target identification activities. We are applying our product engine to discover drug targets to modulate gene expression and develop product candidates for the potential treatment of the root cause of the disease. We plan to utilize our product engine to complete four new drug target identification screens in 2019 and an additional six screens in 2020, and we expect to advance the most compelling programs identified for development.
- **Further expand our product engine capabilities.** Our product engine incorporates patient-derived cell lines and/or other relevant human cell lines, our annotated small molecule compound library and customized CRISPR libraries. We intend to further expand our product engine capabilities, including FulcrumSeek, to enhance the therapeutic reach and productivity of our drug discovery process.
- **Maximize the commercial potential of our product candidates.** We have retained all rights to our lead product candidates focused on rare genetically defined diseases, and plan to commercialize any approved product using a targeted sales infrastructure. We may in the future pursue commercialization partnerships for certain product candidates and/or markets outside the United States.

- **Selectively enter into strategic partnerships to maximize the value of our product engine and pipeline.** Given the breadth of opportunities for our proprietary product engine to discover drug targets and develop product candidates for genetically defined diseases, we may enter into strategic partnerships for certain drug targets, product candidates or disease areas. Partnerships may provide an attractive avenue for expanding the impact of our proprietary product engine.

Gene Regulation

The human genome provides the blueprint, or genetic code, for life. The sequencing of the human genome has enabled significant insights into understanding the genetic underpinnings of many diseases. Genes are the fundamental units of biology, but the gene itself is rather static. The identity and function of each cell is determined by a specific set of factors that activate or repress mechanisms that regulate genes in the desired manner. There are many mechanisms that control the human genome by up or down regulating gene expression, and these regulatory mechanisms are controlled by various pathways and signals. Defects in a gene or any of these regulatory mechanisms can result in aberrant expression or silencing of a gene that may lead to disease.

The graphic below illustrates the key steps in the gene expression process in cells and how they are under the control of a variety of regulatory signals and pathways.



Our Opportunity

We have the ability to develop, scale and characterize complex cellular models of human disorders of gene mis-regulation. Our current drug target identification and development efforts are focused on rare neuromuscular disorders, hemoglobinopathies and CNS diseases. We also anticipate utilizing our product engine to discover drug targets for genetically defined diseases in other therapeutic areas. Our target identification and validation process provides a systematic way to approach the identification of unique drug targets that, when activated or inhibited, may increase or decrease gene expression in genetically

defined diseases with the aim of restoring a healthy or functional phenotype. Our product engine is designed to be agnostic to cell type, pathway and therapeutic modality. While our drug target selection process is guided by our strategy to advance small molecule therapeutics that treat the root cause of disease into clinical development, we also may identify drug targets that might be addressable by other treatment modalities, such as antisense oligonucleotides, or ASOs, small interfering RNAs, or siRNAs, or antibodies.

We are continuing to expand our proprietary relational database, FulcrumSeek, which is designed to facilitate the process by which we assess diseases and generate drug target hypotheses through our computational biology expertise. We screen our proprietary small molecule library and customized CRISPR libraries across healthy and diseased human skeletal muscle cells, cardiac muscle cells, brain cells and blood cells. The data from these screens allow us to develop a broader understanding of biology that may be relevant in disease. With the completion of each additional screening, FulcrumSeek increases in size, and our insights and knowledge are further expanded.

According to the NIH there are approximately 7,000 rare, genetically defined human diseases, many of which have inadequate or no approved treatments. We believe that our approach to selecting and modeling certain of these human diseases with patient-derived tissue-relevant cells, followed by screening with our proprietary small molecule library and customized CRISPR libraries, could be broadly applied to the identification of drug targets that have the potential to balance the expression of many genes known to drive or ameliorate disease.

Our Approach

The ability to intervene in gene regulatory pathways that control gene expression provides the basis of our product engine. Our approach is to broadly search for mechanisms that can change gene expression in the desired manner. These drug targets may be intracellular targets or extracellular targets that affect a signaling pathway. Key considerations we use to determine which genetically defined diseases are suitable to evaluate in drug target identification activities include:

- *Unmet medical need and market opportunity:* we consider the severity of disease, the number of patients who could be treated and the competitive landscape.
- *Clear mechanistic link between a root cause genetic defect and disease:* we evaluate whether there is genetic validation of the gene's role in disease and the effect of gene modulation on disease.
- *Drug discovery execution:* we consider whether relevant patient-derived tissue-specific cell models and assays are available or whether we can develop such models using our expertise.
- *Clinical feasibility:* we evaluate potential biomarker and clinical endpoints, whether there is a meaningful treatment window and whether there is an accessible patient population to undertake clinical trials in a reasonable time frame.

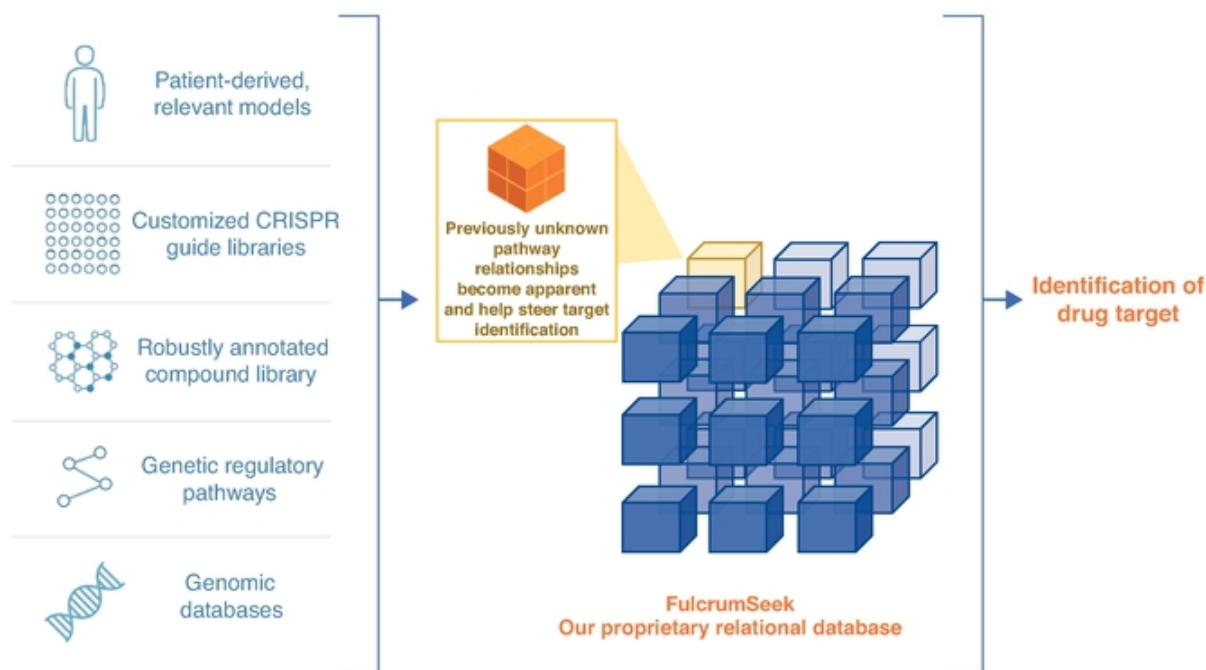
Our product engine is designed to enable us to address diseases in which genes are mis-expressed, silenced or result in mutated gene products, such as RNA or protein, due to an underlying genetic defect. There are varied approaches to treating disease by balancing gene expression including reducing the expression of a gene that causes disease (*e.g.*, *DUX4* in FSHD), increasing the expression of an under-expressed gene (*e.g.*, *FXN* in Friedreich ataxia) or expressing a compensatory gene (*e.g.*, *HBG1/2* in SCD and b-thalassemia). Our preclinical modeling of the relevant tissue is critical for success, and we believe this is best achieved using human cell systems derived from patients with the disease. We primarily seek to identify drug targets that may balance gene expression in these human cell systems and that are amenable to drugging using a small molecule. In addition to drug targets that we prioritize for internal development, we may identify other drug targets that we would consider for development through partnerships.

Overview of Our Product Engine

Our product engine is a high-throughput discovery platform that we designed to identify and validate drug targets that balance the expression of the genes known to drive or ameliorate disease. We employ a systematic methodology that starts with selecting genetically defined diseases with a known root cause. We obtain patient-derived tissue-relevant cell lines or other relevant human cell lines. We then differentiate these cell lines into those most relevant for the disease pathology, including skeletal muscle myotubes, cardiomyocytes, neurons and RBCs, which we then scale up, characterize and prepare for screening. We also generate methods to quantify the desired modulation of expression of the gene of interest in these cell lines. We apply our annotated small molecule compound library and customized CRISPR libraries to the cells to assess for the desired modulation. We confirm drug target hits with multiple modalities and undertake further validation in several patient-derived tissue-relevant cell lines. Additional studies in these cell models are conducted to understand how the modulation of the gene of interest affects cellular function. We employ computational biology using our FulcrumSeek database and other databases to guide drug target selection and generate hypotheses on other drug targets that might be related along a gene regulatory pathway.

To further optimize and increase productivity of our product engine, we have continued to invest in customized lab automation and applied technologies. We believe that these investments have increased assay throughput and robustness and have expanded the breadth of biological parameters we can effectively measure in our assay systems. We believe that we have built a robust product engine to conduct drug target screening at scale in physiologically-relevant assay systems.

We designed our discovery and development model to recapitulate this systematic approach of applying our product engine to each new disease that we evaluate with the goal of providing disease-modifying therapies to patients. The following graphic presents an overview of our drug target identification process.



Patient-Derived Tissue-Relevant Cell Models

Accurate modeling of human disease is critical for drug discovery endeavors, and we have the ability to model disease and identify drug targets that modulate gene expression in patient-derived, differentiated cells. These cells provide the appropriate context in which to understand signaling pathways that affect human gene expression and function, and have the potential to increase the translatability from preclinical studies to clinical trials. Prior to initiating screening activities, we characterize and expand the cells. We also create a cell line where the genetic defect associated with the disease has been corrected, or use a cell line from a healthy individual, in order to compare the gene regulation between diseased and normal cells. If the degree of gene activation or repression required to have a functional benefit is not known, we will undertake physiological characterization of these cell lines in order to define what threshold of gene regulation is functionally relevant.

Our process to characterize patient-derived cell models, produce cells at scale and develop suitable screens to identify drug targets typically takes between six and nine months. Depending on the disease, we may design the screen to measure effects on RNA and/or protein.

Drug Target Identification

We employ three approaches to identify drug targets that can potentially modulate gene expression to treat genetically defined diseases at the root cause—two lab-based library screening approaches as well as computational biology using our FulcrumSeek database and other databases. We then evaluate possible drug targets identified from these efforts with the goal to advance programs into lead optimization.

Small Molecule Probe Library Screening

Our small molecule probe library is annotated, which means it consists of known, well-characterized molecules that interact with biochemical mechanisms and that have cellular activity. The purpose of our small molecule probe library is to identify and interrogate mechanisms that regulate the expression of the gene of interest. We designed our library with the intent to optimize biological diversity, in contrast with other small molecule screening approaches that optimize chemical diversity. The library was developed by our medicinal chemists who reviewed primary and patent literature to identify probe molecules that interact with known biochemical targets. They selected chemical probes based on their cellular activity, potency and selectivity. In order to expand our library beyond commercially-available small molecules, we undertook a custom synthesis campaign to generate compounds that were not available from commercial sources. Our library currently includes more than 4,000 small molecules relating to approximately 2,000 biochemical targets covering a wide breadth of pharmacology, including chromatin modifiers, transcription regulation and RNA processing, kinases and metabolic enzymes. Our library will continue to expand as we identify and acquire new mechanistic probes.

CRISPR Screening

We may also use a customized CRISPR library screening, which is an approach to interrogate the genome by selectively knocking out, reducing or increasing gene expression, for target identification. We have chosen to use CRISPR libraries as complementary or additional screening tools for drug target identification alongside our small molecule screening approach. We use both an array-based CRISPR library and our pooled, custom-designed CRISPR library. Pooled CRISPR screening is an approach to target identification in which we combine cells and reagents in a single tube to simplify the experimental procedures. Pooled CRISPR screening is not suitable for all cell types, and we use array-based CRISPR screening where appropriate. Specific targets that modulate the gene of interest can be identified via CRISPR library screening, and these targets can then be validated for our drug discovery endeavors. If small molecules that interact with these targets are identified from the literature, they are then obtained for further pharmacological validation. If no known chemical matter is available, we may establish a screen

to identify chemical matter that interacts with the drug target. This chemical matter would serve as a starting point for medicinal chemistry work. Alternatively, we may seek partnerships for development using other modalities.

FulcrumSeek and Computational Biology

The primary role of FulcrumSeek and our computational biology capabilities is to generate drug target and biomarker hypotheses using externally generated patient data and internal screening data. Our approach is to leverage our network biology capabilities and expertise to determine how pathways interact with each other in a cell, to develop a network map of regulatory interactions that control gene expression and cellular function and propose targets that potentially could be pursued to address the root cause of diseases of interest. In each case, we explore these hypotheses through biological experimentation designed to validate predicted drug targets and biomarkers. We use confirmatory studies to aid in the refinement of our computational models in an iterative manner.

Drug Target Validation

Our initial focus on drug target validation is to establish a robust link between the drug target that we identified through our screening approaches and modulation of the expression of the root cause gene of interest. Our validation work seeks to evaluate identified drug targets in a manner that allows us to prioritize targets where we may be able to deliver safe and effective therapies to patients. We conduct our validation tests using a diverse set of pharmacological tools and multiple genetic reagents to profile their effect on orthogonal read-outs of gene expression (RNA and protein) and the subsequent effects on physiological function.

The important elements of our systematic approach to drug target validation include:

- *Evaluation of different treatment modalities to interact with the drug target:* we evaluate whether small molecules and genomic modulation approaches similarly affect expression of the gene of interest.
- *Efficacy:* we attempt to establish a link between the identified drug target and the level of the expression of the gene of interest.
- *Safety:* we evaluate whether modulation of the target and the resulting changes in gene expression cause undesired effects, including an assessment of cell health markers to ensure there is minimal cellular toxicity.
- *Profiling cell lines from multiple patients:* we analyze the modulation of the drug target to determine whether the original cell line used to screen targets is representative of disease in other patients.
- *Verification:* we conduct studies designed to ensure that the modulation of the drug target and the resulting change in gene expression leads to a desired functional effect.
- *Prioritization:* we prioritize drug targets based on our assessment of our ability to deliver a candidate for clinical development based on that target.

Development Candidate Discovery and Characterization

Following target identification and target validation, we initiate medicinal chemistry and drug discovery activities to advance a development candidate that is suitable for testing in clinical trials. This work optimizes characteristics that are important for an orally available small molecule, including potency, selectivity, pharmacokinetic, or PK, and safety parameters. There is an opportunity to bypass or considerably accelerate discovery and characterization activities if we identify and validate an attractive drug target that has been pursued previously by others in different indications. For example, available chemical matter and support from the scientific literature regarding p38a/b enabled us to rapidly identify our product candidate for the treatment of FSHD.

A key element of our preclinical compound profiling approach is to investigate a development candidate across many patient-derived tissue-relevant cells. We choose these cells based on our assessment of the patient heterogeneity that may be encountered in clinical trials. The purpose of this analysis is to enable us to understand if the activity of the molecule differs among cells with different genetic subtypes, or if a patient stratification strategy is appropriate for clinical trials.

Many genetically defined diseases are not well modeled with animal models because such models do not have appropriate predictive validity. In these cases, we seek to develop an engraftment model where patient-derived human cells are engrafted into the relevant tissue of a host, immunodeficient mouse to produce a chimeric mouse. We may use these chimeric mice to assess gene regulation in the engrafted human cells, and for the efficient development of PK-pharmacodynamic, or PK/PD, relationships that will be the basis of therapeutic index calculations and human dose projections.

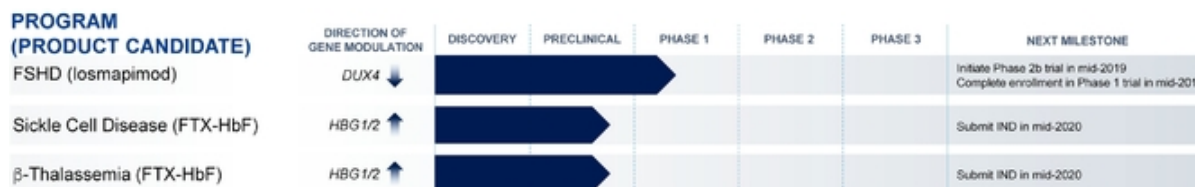
Advantages of a Small Molecule Approach

We believe that our approach to the treatment of genetically defined diseases using orally available, small molecule therapeutics may offer significant advantages over other treatment modalities due to:

- **Biodistribution:** small molecules can achieve broad distribution in the body. The ability to access tissues broadly is particularly relevant in neuromuscular disorders where multiple muscles are affected by disease, or in CNS diseases where brain permeability may be limited with other treatment modalities.
- **Tolerability:** small molecules have a limited risk of immunogenicity and lack procedural risk relative to administering other treatment modalities, such as ASOs and gene therapies.
- **Manufacturing and quality:** the production and quality control of drug supplies for clinical development are well understood. Specialized facilities are generally not required, and many vendors offer services for manufacturing. We believe small molecule manufacturing may provide cost advantages relative to other modalities.
- **Patient access:** small molecule, oral medicines can be administered by the patient and do not require complicated in-patient procedures that are sometimes only available in a limited number of treatment centers.

Our Lead Product Candidates

We have used our proprietary product engine and screening efforts to identify drug targets for our lead product candidates. We in-licensed our first product candidate, losmapimod, after we discovered that it could reduce aberrant expression of the *DUX4* gene, which is the known root cause of FSHD. We expect to initiate a randomized Phase 2b clinical trial in mid-2019. We designed our second product candidate, FTX-HbF, to upregulate fetal hemoglobin, which we believe would compensate for abnormal hemoglobin in SCD and certain types of β -thalassemia. We aim to submit an IND for FTX-HbF in mid-2020. The following chart summarizes key information about our lead product candidates.



Our Product Candidate for Facioscapulohumeral Muscular Dystrophy

Overview of Facioscapulohumeral Muscular Dystrophy

Facioscapulohumeral muscular dystrophy is a rare, progressive and disabling disease for which there are no approved treatments. FSHD is one of the most common forms of muscular dystrophy and affects both sexes equally, with onset typically in teens and young adults. FSHD is characterized by progressive skeletal muscle loss that initially causes weakness in muscles in the face, shoulders, arms and trunk and progresses to weakness in muscles in lower extremities and the pelvic girdle. Skeletal muscle weakness results in significant physical limitations, including progressive loss of facial muscles that can cause an inability to smile or communicate, difficulty using arms for activities of daily living and difficulty getting out of bed, with many patients ultimately becoming dependent upon the use of a wheelchair for daily mobility activities. The majority of patients with FSHD also report experiencing chronic pain, anxiety and depression. The diagnosis and treatment of patients with FSHD is typically performed by neurologists.

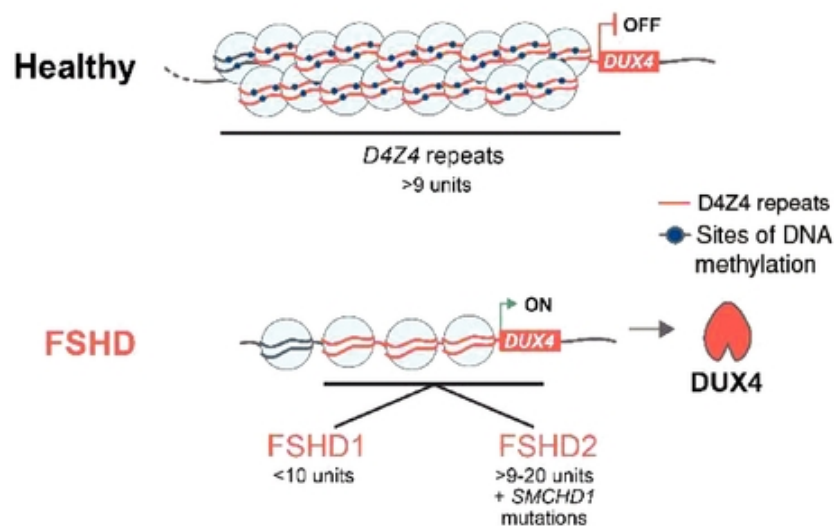
The FSH Society estimated that the prevalence of FSHD in the United States is approximately 1 in 20,000 people. A recent study conducted in the Netherlands reported a more frequent prevalence of 1 in 8,333. Based on these estimates and a U.S. population of 320 million, we estimate that the patient population is between 16,000 to 38,000 in the United States. We believe that there may be additional patients who are not formally diagnosed due to a perceived difficulty of obtaining a diagnosis and the fact that there are no approved treatments. Approximately two-thirds of cases are familial-inherited in an autosomal dominant fashion and one-third of cases are sporadic. FSHD affects all ethnic groups with similar incidence and prevalence.

FSHD Biology

FSHD is caused by aberrant expression of *DUX4* in skeletal muscle resulting in the inappropriate presence of DUX4 protein, a transcription factor causing the expression of other genes. Normally DUX4-driven gene expression is limited to early embryonic development, after which time the *DUX4* gene is silenced. In patients with FSHD, aberrant production of DUX4 protein in skeletal muscle regulates other genes encoding proteins, some of which are toxic to the muscle. Evidence of aberrant DUX4-driven gene expression is the major molecular signature that distinguishes muscle tissue affected by FSHD from healthy muscle. The result of aberrant *DUX4* expression in FSHD is death of muscle and its replacement by fat, resulting in skeletal muscle weakness and progressive disability. We believe that reducing expression of the *DUX4* gene and its downstream transcriptional program could provide a disease-modifying therapeutic approach for the treatment of FSHD at its root cause.

In all patients with FSHD, the *DUX4* gene is unsilenced, or de-repressed, as a result of one of two different types of genetic alterations, leading to FSHD1 or FSHD2. Approximately 95% of patients have FSHD1 and approximately 5% of patients have FSHD2. FSHD1 is caused by the contraction of an array of DNA, known as a D4Z4 repeat, from greater than ten repeat units to nine or fewer units. This contraction causes de-repression of *DUX4*. Patients with FSHD2 do not have meaningful D4Z4 repeat contraction, but have mutations in a regulatory gene, known as the *SMCHD1* gene, that normally contributes to the repression of the *DUX4* gene via DNA methylation.

The figure below illustrates how genetic mutations in the D4Z4 repeat array (FSHD1) or the *SMCHD1* gene (FSHD2) result in aberrant expression of *DUX4* in skeletal muscle.



Our Product Engine Identified the Drug Target for FSHD

We utilized patient-derived FSHD1 muscle cells, known as myotubes, and screened them with our small molecule probe library to identify drug targets that reduced *DUX4* expression. We identified several potential drug targets, however the modulation of the majority of the targets adversely affected the health or differentiation of muscle cells. One drug target that we identified from our screening efforts for which we did not observe adverse cell health issues was p38a/b, which had been studied extensively in other diseases, but had not been reported to be linked to *DUX4* expression or FSHD until we conducted our screening efforts. We evaluated multiple small molecule p38a/b inhibitors and observed a consistent reduction of both *DUX4* expression and *DUX4*-driven gene transcripts with each p38a/b inhibitor. We conducted further validation experiments to confirm that inhibition of p38a using genetic approaches such as siRNA and CRISPR single-guide RNAs, also led to a reduction in *DUX4* expression.

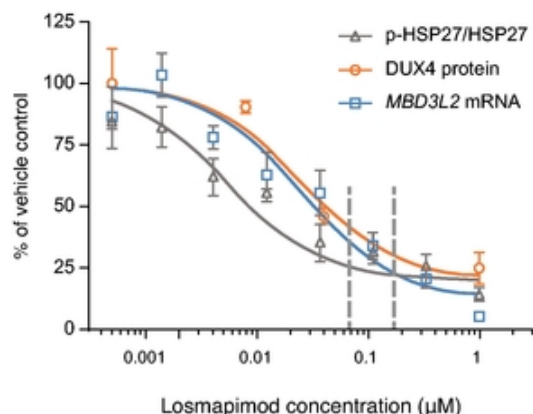
Losmapimod

After identifying p38a/b as a potential drug target, we evaluated multiple small molecule inhibitors of p38a/b. Each of these inhibitors had previously been evaluated in clinical trials for the treatment of various diseases but never in muscle disorders. As a result of our evaluation and relative to other p38a/b inhibitors, we identified losmapimod as the preferred development candidate based on substantial and attractive preclinical and clinical data regarding safety, PK and target inhibition, and its advanced stage of development. Losmapimod was originally evaluated by GSK in nearly 3,500 subjects in clinical trials across multiple indications and in multiple countries. GSK did not evaluate losmapimod in FSHD or in any other muscle disorder. Although GSK did not pursue regulatory approval in the indications evaluated, losmapimod demonstrated an attractive PK, PD, safety and tolerability profile, including in chronic dosing.

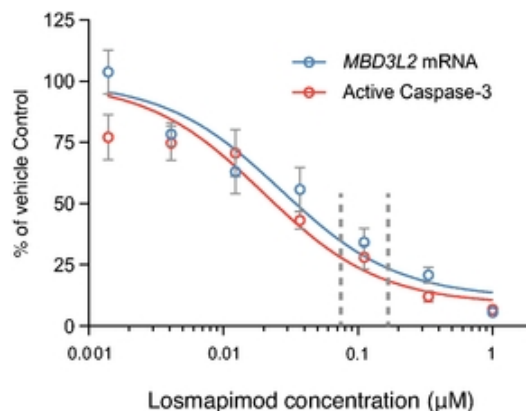
As shown in the figure on the left below, we observed in preclinical studies using losmapimod that inhibition of the p38a/b pathway reduced *DUX4* expression and downstream gene expression, as measured by the mRNA transcribed by *MBD3L2*, a gene that is only expressed following *DUX4* activation. In the study, we demonstrated that *MBD3L2* was representative of broader *DUX4*-driven gene expression changes in myotubes. We assessed the ability of losmapimod to inhibit p38a/b by measuring the effect on the phosphorylation of a downstream protein called heat shock protein 27, or HSP27. The level of phosphorylation of HSP27 has been used in previous clinical trials, including by GSK, as a biomarker to

measure the degree of p38a/b inhibition. As shown in the figure on the right below, we also observed reduced cell death, or apoptosis, in FSHD myotubes, as measured by active caspase-3. We used active caspase-3 to quantify cell death because it is a protein that has been shown to be an important regulator of the apoptosis pathway in myotubes.

Losmapimod reduced DUX4 protein levels and DUX4-driven gene expression



Losmapimod reduced apoptosis in FSHD myotubes



The dotted lines in each graphic above indicate the Cmin (left) and Cmax (right) observed in a clinical trial conducted by GSK that used a 15 mg twice per day dose of losmapimod. Cmin represents the minimum concentration in plasma prior to administration of a subsequent dose and Cmax represents the highest concentration in plasma after administration of a dose.

After identifying losmapimod, we in-licensed the molecule from GSK because we believed that its safety and pharmacology history would significantly expedite our development plan and enhance our future regulatory submissions. In February 2019, we obtained an exclusive worldwide license from GSK to the losmapimod patents and preclinical and clinical data for all indications, subject to certain conditions. This license includes a letter of reference for the U.S. Food and Drug Administration, or FDA, providing us the right to reference all the previous INDs that had been filed by GSK for losmapimod, as well as a license to their losmapimod data, including the original preclinical study and clinical trial reports. We also received active pharmaceutical ingredient, or API, and losmapimod tablets that had been manufactured by GSK. We plan to use the API and tablets to support our clinical development of losmapimod in FSHD, including our planned Phase 2 clinical trials. We utilized the GSK data and our preclinical data to submit an IND in the United States and CTAs in Europe and Canada in May 2019 that will enable us to advance our clinical development plan for losmapimod in FSHD, including initiating a Phase 2b clinical trial. The IND was accepted by the FDA in June 2019.

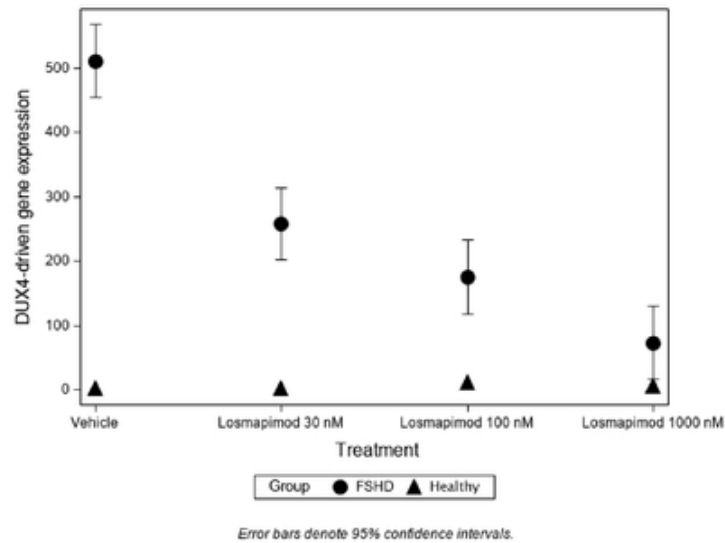
Preclinical Development

We conducted several preclinical studies designed to evaluate the ability of losmapimod to reduce DUX4-driven gene expression. In a preclinical study of losmapimod, we treated myotubes from primary cell lines of eight FSHD1 and three FSHD2 patients for four days with different concentrations of losmapimod or vehicle as a negative control. To model the effect of losmapimod treatment on DUX4-driven gene expression across diverse disease-causing genotypes, we measured *MBD3L2* transcript levels relative to the transcript levels of *POLR2A*, a gene whose expression is not regulated by DUX4 protein. We observed that clinically achievable concentrations of losmapimod (30 to 100 nM) decreased DUX4-driven expression by 50% to 65%, as measured by quantitative polymerase chain reaction amplification of the *MBD3L2* transcripts. The observed treatment effect was similar in all cells tested.

regardless of genotype. We believe that this data suggests that losmapimod has the potential to treat FSHD patients across all genotypes.

The graphic below shows the least square mean estimates for DUX4-driven gene expression from 11 FSHD primary cells and healthy cells treated with losmapimod presented as mean and 95% confidence intervals, which demonstrates that losmapimod reduced DUX4-driven gene expression, as measured by MBD3L2 and POLR2A transcript levels in a concentration-dependent manner.

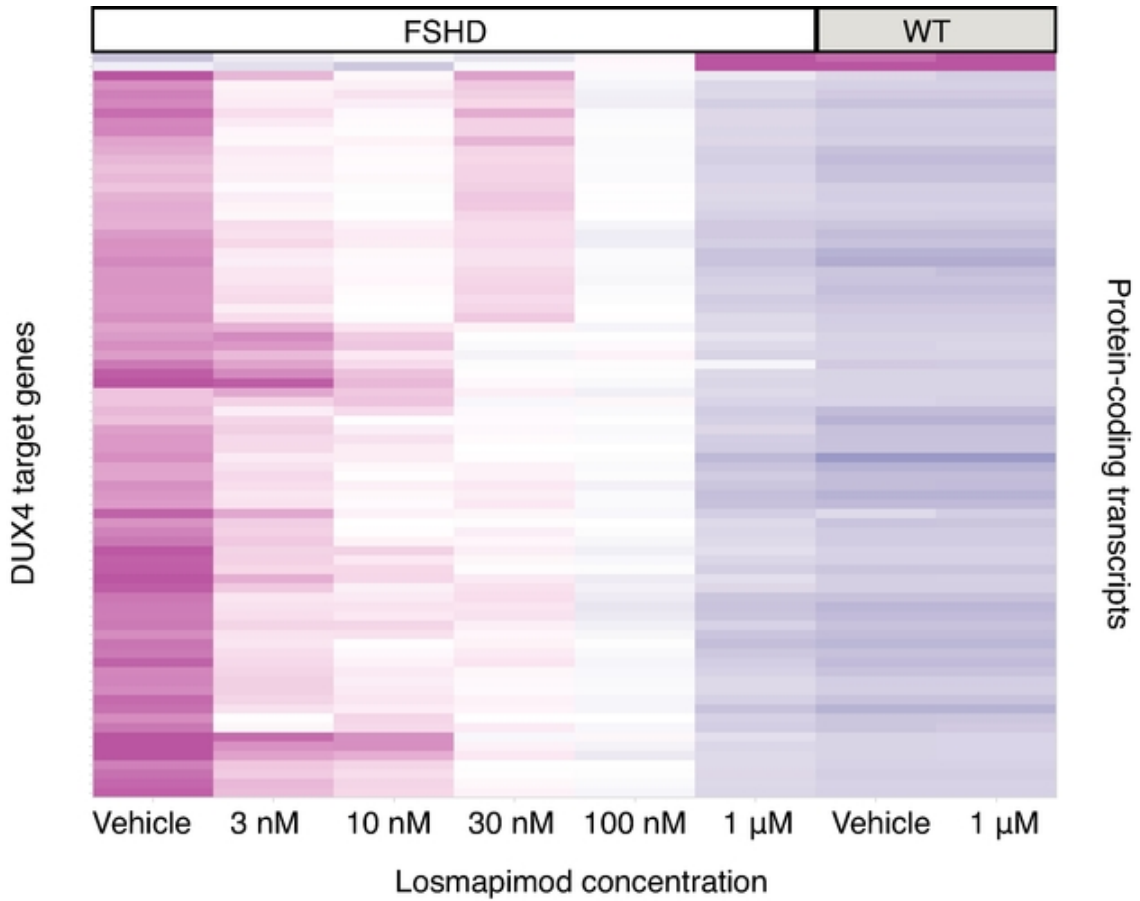
Reduction of DUX4-driven gene expression at increasing concentrations of losmapimod



In our preclinical studies, we have also observed that treatment of FSHD patient-derived myotubes with losmapimod is highly specific for DUX4-driven gene expression. We conducted a study in which we measured the FSHD gene expression signature and observed a minimal impact on myogenesis when healthy human myotubes were treated with losmapimod. We treated FSHD cells with losmapimod for five days and a subsequent RNA-seq analysis revealed that only 89 transcripts (0.45%) out of approximately 20,000 protein coding genes were differentially expressed more than four-fold. Of these 89 differentially expressed transcripts, 90% were transcripts directly regulated by DUX4. We believe that this is strong evidence that the effects of losmapimod in affected skeletal muscle are highly specific for the treatment of the root cause of FSHD. Importantly, we did not observe changes in levels of myogenin, a transcriptional activator that promotes transcription of muscle-specific genes and plays a role in muscle differentiation, cell cycle exit and muscle atrophy, and observed minimal impact on other myogenic factors during myoblast differentiation into myotubes.

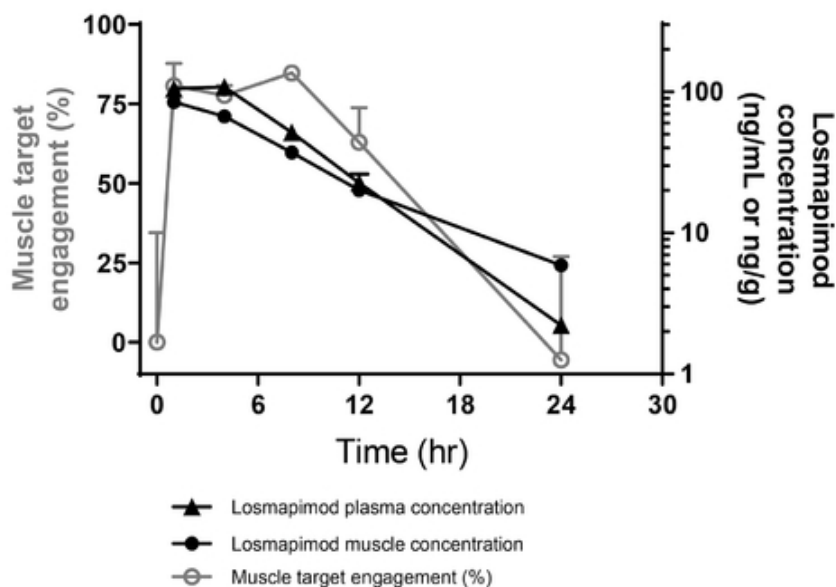
The graphic below depicts the gene expression signature in FSHD at increasing concentrations of losmapimod as compared to a high concentration of losmapimod in healthy wild type, or WT, myotubes. In

the graphic, darker pink tones indicate more gene expression and darker blue tones indicate less gene expression.



GSK observed concentrations of losmapimod in human plasma of 28.4 ng/mL to 74.1 ng/mL with an average of 50.5 ng/mL at a 15 mg twice per day dose in its clinical trials. In preclinical studies in animal models, we observed that losmapimod reached muscle tissue and engaged the p38a/b target in the muscle tissue. As shown below, we detected similar concentrations of losmapimod in rat plasma and muscle, and significant target engagement is observed at concentrations that we expect to achieve in clinical trials using a 15 mg twice per day dose.

p38a/b target engagement over time



We obtained further evidence that losmapimod distributed to muscle from a preclinical study in which GSK profiled distribution of losmapimod to all tissues in rats. Our review of this data similarly confirmed that muscles were well exposed to losmapimod.

Clinical Development Overview

We began dosing in a Phase 1 clinical trial of losmapimod in healthy volunteers and patients with FSHD in Europe in February 2019 following the filing of a CTA in December 2018. We plan to conduct a randomized, double-blind placebo-controlled Phase 2b clinical trial with approximately 66 patients with FSHD to investigate whether oral administration of 15 mg of losmapimod twice per day reduces expression of DUX4-driven genes in affected skeletal muscle. We also plan to concurrently conduct an open label Phase 2 clinical trial in 16 patients with FSHD to investigate the safety and tolerability of 15 mg losmapimod twice per day for chronic use and to evaluate the ability of losmapimod to reduce expression of DUX4-driven genes in affected skeletal muscle over varying durations of treatment. We believe that a 15 mg twice per day dose of losmapimod is an appropriate dose for the treatment of patients with FSHD based on previous clinical data and p38a/b target engagement data generated by GSK and p38a/b target engagement data from our preclinical studies.

We submitted a CTA in Europe for the open label Phase 2 clinical trial in April 2019 and submitted CTAs in Europe and Canada for the Phase 2b clinical trial in May 2019. The FDA accepted the IND in June 2019. We expect to initiate the randomized Phase 2b clinical trial and the open label Phase 2 clinical trial in mid-2019.

We are also conducting several preparatory non-drug studies to assess biomarker endpoints and clinical outcome assessments. In addition, we are participating in a natural history study that will follow 150 subjects with FSHD in the United States and 70 subjects in Europe over 18 months. We expect to utilize the data generated from our non-drug studies and the natural history study to inform discussions with regulatory agencies and future clinical trial design.

We believe that the safety data from GSK's prior losmapimod clinical trials, together with safety and efficacy data from our Phase 1 and Phase 2 clinical trials, may enable us to apply for accelerated approval. We believe a treatment for FSHD may be eligible for accelerated approval because FSHD is a rare, slowly progressive and disabling disease with no approved treatments. We plan to discuss accelerated approval with regulatory agencies if we observe positive results in our Phase 2b clinical trial based on biomarker

endpoints that we believe are likely to predict clinical benefit. We also plan to apply for orphan drug designation for FSHD in the United States and Europe in 2019.

Prior Clinical Development of Losmapimod by GSK

GSK conducted multiple Phase 1 and Phase 2 clinical trials and one Phase 3 clinical trial of losmapimod, including in patients with chronic obstructive pulmonary disease, or COPD, acute coronary syndrome and other cardiovascular diseases, neuropathic pain, major depression disorder, focal segmental glomerulosclerosis, and rheumatoid arthritis. Nearly 3,500 subjects in 24 trials were given losmapimod with single doses as high as 60 mg and repeated oral doses as high as 15 mg twice per day for up to 52 weeks. We plan to use a dose of 15 mg twice per day in our clinical trials of losmapimod in FSHD. GSK did not conduct a clinical trial of losmapimod in patients with FSHD or any other muscle disorder.

In clinical trials of losmapimod conducted by GSK, no significant differences were observed in the frequency of adverse events, or AEs, in subjects given losmapimod and subjects given placebo. GSK generally observed a similar frequency of serious adverse events, or SAEs, and deaths between patients given losmapimod and patients given placebo. These trials included extensive evaluation of the cardiovascular risk profile of losmapimod, including completion of an evaluation of the potential to prolong corrected QT. GSK reported that there was no clinically relevant difference with regard to the occurrence of electrocardiogram abnormalities post-baseline or vital signs with losmapimod as compared to placebo. GSK did not identify a safety signal attributed to losmapimod in any of these trials. There were no SAEs reported in 14 of these 24 clinical trials of losmapimod.

The table below presents safety data from the largest placebo-controlled clinical trial of losmapimod, which was a Phase 3 clinical trial for the treatment of acute coronary syndrome following a heart attack, in which over 1,700 patients were given 7.5 mg of losmapimod or placebo twice per day for 12 weeks and were followed for an additional 12 weeks. In this trial, GSK observed a similar proportion of AEs in the placebo group as compared to the losmapimod group. The data in the table below presents the SAEs reported by more than 0.5% of patients in any group in the trial through 24 weeks.

Safety data from GSK's Phase 3 clinical trial of losmapimod in patients with acute coronary syndrome		
	Placebo	Losmapimod
	N = 1,752	N = 1,724
	n (%)	n (%)
Any SAE	323 (18.4)	363 (21.1)
Cardiac disorders	114 (6.5)	138 (8.0)
Infections and infestations	54 (3.1)	55 (3.2)
Respiratory, thoracic and mediastinal disorders	24 (1.4)	41 (2.4)
General disorders and administration site conditions	35 (2.0)	26 (1.5)
Renal and urinary disorders	18 (1.0)	31 (1.8)
Investigations	28 (1.6)	18 (1.0)
Musculoskeletal and connective tissue disorders	14 (0.8)	25 (1.5)

There were also ten fatal SAEs in the placebo group and 13 fatal SAEs in the losmapimod group. In the placebo group, the fatal SAEs were infections and infestations (two), general disorders and administrative site conditions (two), respiratory, thoracic and mediastinal disorders (three), cardiac disorder (one), gastrointestinal disorder (one) and neoplasm (one). In the losmapimod group, the fatal SAEs were infections and infestations (four), general disorders and administrative site conditions (three), respiratory, thoracic and mediastinal disorders (two), cardiac disorder (one), injury poisoning and procedural complications (one), gastrointestinal disorder (one) and neoplasm (one).

The following table presents SAEs reported during treatment from a total of 11 Phase 1 and Phase 2 placebo-controlled clinical trials of losmapimod with repeat dosing for which GSK reported integrated data. The 11 trials presented include three of the 14 trials in which no SAEs were reported.

Safety data from 11 clinical trials of losmapimod conducted by GSK		
	Placebo	Losmapimod
	N = 735	N = 1,327
	n (%)	n (%)
Any SAE	47 (6)	120 (9)
Cardiac disorders	17 (2)	41 (3)
Respiratory, thoracic and mediastinal disorders	11 (1)	26 (2)
Infections and infestations	7 (<1)	14 (1)
General disorders and administrative site conditions	7 (<1)	13 (<1)
Nervous system disorders	5 (<1)	10 (<1)
Injury, poisoning and procedural complications	1 (<1)	11 (<1)
Gastrointestinal disorders	1 (<1)	7 (<1)
Vascular disorders	1 (<1)	5 (<1)
Renal and urinary disorders	2 (<1)	4 (<1)
Musculoskeletal and connective tissue disorders	2 (<1)	4 (<1)
Skin and subcutaneous tissue disorders	2 (<1)	4 (<1)
Hepatobiliary disorders	0	4 (<1)
Psychiatric disorders	2 (<1)	3 (<1)
Neoplasms (benign, malignant and unspecified)	1 (<1)	3 (<1)
Blood and lymphatic system disorders	0	1 (<1)
Immune system disorders	0	1 (<1)
Metabolism and nutrition disorders	0	1 (<1)

This table includes safety data from the second largest clinical trial of losmapimod, which was a placebo-controlled Phase 2 clinical trial of losmapimod in patients with COPD, in which 602 adult patients were given 2.5 mg, 7.5 mg or 15 mg of losmapimod or placebo twice per day for 24 weeks and were followed for an additional week. In this trial, GSK observed a similar proportion of AEs in the placebo group as compared to the losmapimod group. Additionally, in this trial there were three fatal SAEs in the placebo group due to severe exacerbation of COPD, acute myocardial infarction and pulmonary embolism, one fatal SAE in the losmapimod 7.5 mg group due to acute myocardial infarction and associated pulmonary edema and two fatal SAEs in the 15 mg group due to respiratory failure and bilateral purulent pleuritis and mediastinitis. The most common SAE observed in the trial was exacerbation of COPD, which was experienced by eight subjects in the placebo group, six subjects in the losmapimod 2.5 mg group, two subjects in the losmapimod 7.5 mg group and three subjects in the losmapimod 15 mg group. Other SAEs in the placebo group included a liver event, eczema, leukoplakia, sinobronchitis and anxiety. Other SAEs in the losmapimod groups included two subjects with liver events, one subject with eczema and leukoplakia, one subject with pyrexia and one subject with pemphigoid.

In addition to the trials and data summarized above, GSK also conducted a placebo-controlled Phase 2 clinical trial in which 184 adult patients with frequently exacerbating COPD were given 15 mg of losmapimod or placebo twice per day for up to 52 weeks. In this trial, the proportion of subjects with AEs and SAEs was higher in the losmapimod group than in the placebo group; there was one fatal SAE in the

placebo group and three fatal SAEs in the losmapimod group, none of which was considered related to losmapimod. The data in the table below presents the SAEs reported in the trial.

Safety data from GSK's Phase 2 clinical trial of losmapimod in patients with COPD		
	Placebo	Losmapimod
	N = 94	N = 90
	n (%)	n (%)
Any SAE	8 (9%)	18 (20%)
Respiratory, thoracic and mediastinal disorders	2 (2)	7 (8)
Cardiac disorders	3 (3)	4 (4)
Infections and infestations	1 (1)	6 (7)
Injury, poisoning and procedural complications	1 (1)	2 (2)
Neoplasms (benign, malignant and unspecified)	2 (2)	1 (1)

In addition to the 24 trials conducted by GSK, another sponsor conducted a placebo-controlled Phase 2 clinical trial of losmapimod in which 73 subjects with COPD with cardiovascular manifestations were given 7.5 mg of losmapimod or placebo for 16 weeks. There were 36 subjects in the losmapimod group and 37 in the placebo group. In this trial, there were a total of six (17%) SAEs in the losmapimod group, consisting of exacerbations of COPD and pneumonia, and there was one (3%) SAE in the placebo group.

In prior studies, GSK observed that the p38a/b target inhibition in humans was approximately 10%, 30% and 50% at trough and 40%, 60% and 70% at peak following twice per day doses of 2.5 mg, 7.5 mg and 15 mg, respectively. In addition, based on *in vitro* data from our studies in FSHD myotubes with losmapimod, we believe that the muscle exposures that we have achieved in rodents, which are similar to concentrations in human blood from the 15 mg twice per day dose, will result in robust p38a/b target engagement and will reduce DUX4-driven gene expression in FSHD skeletal muscle by more than 50%. We believe that this data supports our determination that 15 mg of losmapimod twice per day is an appropriate dose for the treatment of patients with FSHD.

*Our Clinical Development Strategy**Preparatory Studies*

There are currently four ongoing preparatory studies designed to inform molecular biomarker and clinical development efficacy endpoints for planned clinical trials of losmapimod in patients with FSHD.

Study	Subjects (Planned)	Description / Endpoints
Biomarker Preparatory Study (Fulcrum SRA 002-2018)	18	DUX4-driven gene expression in skeletal muscle and whole-body skeletal muscle MRI
Optimized Time Up and Go Test Preparatory Study (Fulcrum SRA 003-2018)	22	Optimized time up and go test for FSHD, or FSHD-TUG
Direct Patient Input (Fulcrum SRA 004-2018)	100	Direct patient input into the Phase 2b clinical trial
ReSOLVE Natural History Study (NIH) and Reachable Work Space (Fulcrum SRA 003-2017)	150	Natural history study Reachable work space
EU Natural History Study and Reachable Work Space (SRA 003-2017)	70	Natural history study Reachable work space

Biomarker Preparatory Study (Fulcrum SRA 002-2018)

We designed this preparatory study to investigate, inform and optimize the DUX4-driven gene expression and MRI efficacy biomarker endpoints that we intend to use in clinical trials of losmapimod. We are evaluating 18 subjects at seven clinical sites. We completed enrollment in May 2019 and will use the data to inform our planned Phase 2 trials of losmapimod for the treatment of FSHD.

This preparatory study is designed to measure aberrant DUX4-driven gene expression in affected skeletal muscle via a subset of DUX4-driven gene transcripts in order to develop a molecular muscle endpoint designed to track the root cause of disease. We are using MRI to inform affected leg muscles selected for biopsy. We believe that the measurement could be a primary endpoint in a clinical trial to support accelerated approval of losmapimod for FSHD. We are also using whole-body MRI scans one to three months apart to evaluate changes in skeletal muscle health (lean muscle tissue volume and muscle tissue replaced by fat).

The subjects have clinical severity scores of two to four on the Ricci scale, which is the clinical impairment disability scale for patients with FSHD, where a zero indicates that a subject has no disability and five indicates that a subject is permanently dependent upon the use of a wheelchair for daily mobility activities.

Optimized Time Up and Go Test Preparatory Study (Fulcrum SRA 003-2018)

We are evaluating a modified version of the classic time up and go, or classic TUG, test that we are optimizing as a clinical outcome assessment of mobility and ambulation, which we refer to as the FSHD-TUG test. The classic TUG test requires patients to get up from a chair, walk three meters, turn around, walk back to the chair and sit down. It was originally developed for clinical practice to assess mobility, balance, walking ability and fall risk in older adults prior to discharge from hospitalization and

was used recently as a key secondary efficacy endpoint in a registration trial in multiple sclerosis in Europe. The classic TUG test is also one of the clinical outcome assessments in the ReSOLVE natural history study discussed below.

While we believe that the classic TUG test is a valid, reliable and objective test to quantify functional mobility in all age groups, we believe that a minor modification, asking patients to get up from a standardized bed, will be more appropriate for FSHD patients. We believe that the FSHD-TUG test may be more sensitive to measure treatment effects in patients with FSHD. Patients with FSHD generally have a difficult time rising from a chair and even more so from a recumbent position and this difficulty progresses over time. Patients with FSHD report that limitations in mobility and in the use of the shoulders and upper arms are the two most important areas of concern. The FSHD-TUG test may be a useful clinical outcome assessment endpoint for measurement of treatment effects of losmapimod on mobility.

We are currently testing the FSHD-TUG test in comparison to the classic TUG test in a group of 22 subjects with FSHD and in 20 healthy volunteers who are age and gender matched. The subjects will have clinical severity scores of one to four on the Ricci scale. We are evaluating the subjects in five visits over approximately 12 months.

Direct Patient Input (Fulcrum SRA 004-2018)

We are also seeking to obtain direct patient input into the design and feasibility of our planned Phase 2b clinical trial by having approximately 100 patients with FSHD complete a survey based on their review of the proposed schedule of clinical outcome assessments for the trial. The patients will provide their views on their willingness to participate and any potential barriers to their participation in our planned Phase 2b clinical trial. We conduct these surveys during a face-to-face interview in clinics in the United States and France, via an internet survey for members of an FSHD registry in the United Kingdom and through in-person groups in Canada. We have the ability to refine the protocol for our Phase 2b clinical trial to reflect the feedback from patients.

ReSOLVE Natural History Study

The Clinical Trial Readiness to Solve Barriers to Drug Development in FSHD, or ReSOLVE study, is an ongoing natural history study funded by the NIH to help identify the patient population, efficacy biomarker and clinical outcome assessments for future FSHD drug trials. The study is being coordinated by the University of Rochester and University of Kansas Medical Center and enrolled the first subject in April 2018. The study will follow approximately 150 subjects for 18 months across a network of eight U.S. clinical centers and will evaluate multiple biomarkers and clinical outcome assessments that may be suitable for clinical trials and will evaluate patient selection criteria based on genetic, demographic or clinical characteristics. Three sites in the European Union have joined the ReSOLVE protocol and will follow approximately 70 subjects for 18 months. As of June 2019, over 140 subjects have been enrolled. We believe that the results of this natural history study will inform the design and implementation of clinical trials and will inform discussions with regulatory agencies. We also believe that this study may provide valuable insights into the timeline for disease progression and functional changes in FSHD in the absence of treatment.

In connection with the ReSOLVE study, we have funded the addition of a clinical outcome assessment, which we refer to as reachable work space, or RWS. RWS is an objective assessment of upper arm function in a quantitative manner by measuring arm and shoulder mobility with and without weights. A hallmark of FSHD progression is weakness in the shoulder muscles and upper arms that eventually leads to an inability of patients to lift their arms above their shoulders. The RWS assessments are analyzed by a central reader. We have provided standardized hardware, software, and testing conditions to evaluate RWS at eight sites that are part of the ReSOLVE study in the United States and at three European sites. To date, we have collected over 300 RWS assessments in the study.

Phase 1 Clinical Trial

We are conducting a randomized Phase 1 clinical trial of losmapimod in healthy adult volunteers and patients with FSHD in Europe under a CTA that we filed in December 2018. We expect that this trial will be completed in 2019. We intend to present data in the fourth quarter of 2019 at a scientific conference.

In this trial, we have dosed eight healthy volunteers with 7.5 mg of losmapimod capsules, followed by a washout period, and subsequently dosed the same volunteers with a 15 mg dose of losmapimod capsules. As part of this trial, we have also dosed two healthy volunteers with placebo capsules in both periods. Consistent with the extensive data that we in-licensed from GSK, losmapimod has been well tolerated in this trial.

Following the completion of the healthy volunteer cohort, we began dosing patients with FSHD in April 2019. We plan to enroll up to 20 patients in this trial. This trial is designed to obtain safety and tolerability of losmapimod in patients with FSHD. Patients are being randomized across three arms of 7.5 mg or 15 mg of losmapimod capsules or placebo twice per day for 14 days. We also intend to compare p38a/b target engagement in skeletal muscle of patients treated with a dose of 7.5 mg and 15 mg of losmapimod twice per day relative to that of patients on placebo. We aim to confirm that 15 mg twice per day is the appropriate dose for our Phase 2 trials based on higher muscle exposures and target engagement than the 7.5 mg twice per day dose. We will measure target engagement and other biomarkers in muscle needle biopsies before and after two weeks of treatment.

We manufactured the losmapimod capsules for this trial prior to our license agreement with GSK. For our Phase 2 clinical trials, we will use losmapimod tablets that were manufactured by GSK. We confirmed that the PK of the losmapimod capsules were consistent with published data on the PK of the losmapimod tablets manufactured by GSK. In this trial, we are also confirming that the p38a/b target engagement in blood from our losmapimod capsules is consistent with the previous data on target engagement of the losmapimod tablets manufactured by GSK.

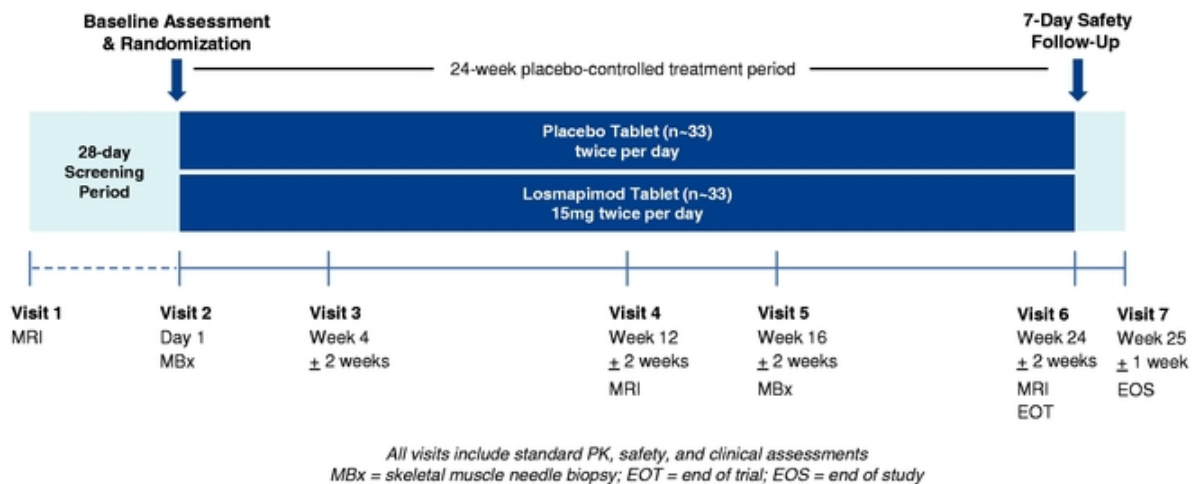
Phase 2b Clinical Trial

We plan to initiate a randomized, double-blind, placebo-controlled Phase 2b clinical trial in approximately 66 patients with FSHD1 and clinical severity scores of two to four on the Ricci scale. In this trial, we will evaluate treatment with 15 mg of losmapimod or placebo tablets twice per day over a 24-week period. Patients will be randomized 1:1 between the treatment and placebo arms. The FDA accepted the IND for losmapimod in June 2019, and we also submitted CTAs in May 2019 to conduct the trial at sites in Europe and Canada and expect to initiate this trial in mid-2019.

The primary endpoint will be the reduction of DUX4-driven gene expression in affected skeletal muscle biopsies before treatment and after approximately 16 weeks of treatment. We selected the number of patients to enroll in this trial based on the magnitude of reduction of DUX4-driven gene expression that we have observed in our preclinical studies using losmapimod concentrations similar to those measured when dosing with 15 mg twice per day in clinical trials completed by GSK.

Secondary endpoints of the trial will include evaluation of safety and tolerability in FSHD patients, PK in blood, losmapimod concentration in skeletal muscle biopsies, and p38a/b target engagement in blood and in muscle biopsies. This trial will also include evaluation of exploratory efficacy endpoints including MRI biomarkers and clinical outcome assessments. The clinical outcome assessments include centrally read RWS, FSHD-TUG test and patient-reported outcomes and muscle strength measured by quantitative dynamometry and motor function ability measurements obtained by physical therapists.

The graphic below presents the design of the Phase 2b clinical trial.



Phase 2 Open Label Clinical Trial

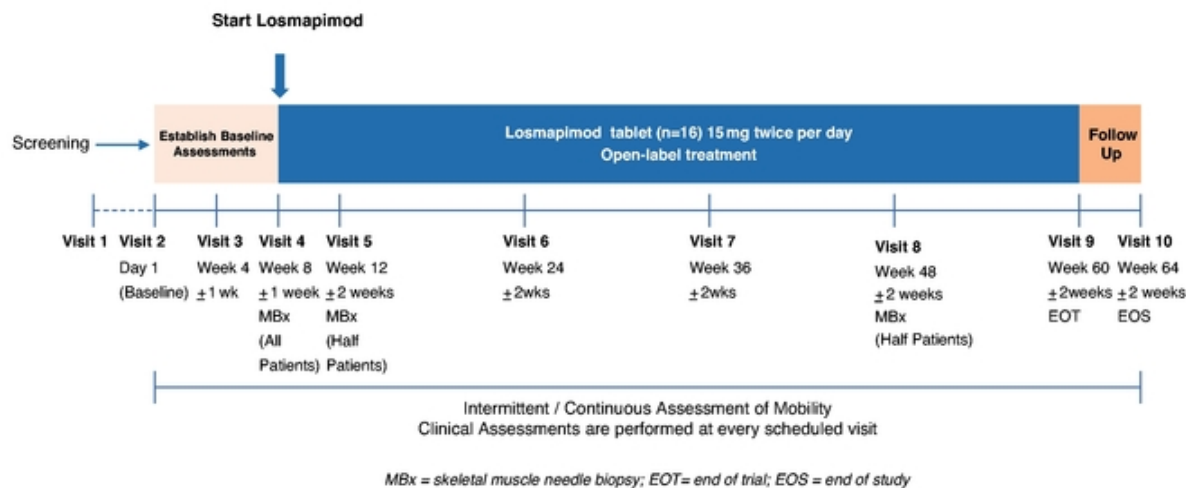
In parallel with the Phase 2b clinical trial, we also plan to initiate enrollment in mid-2019 for an open label, single site Phase 2 clinical trial of losmapimod in 16 patients with FSHD1 and clinical severity scores of two to four on the Ricci scale. Patients will receive tablets containing 15 mg of losmapimod twice per day for up to 52 weeks. The treatment period will be preceded by eight weeks of pre-treatment assessments to establish a baseline for musculoskeletal MRI biomarkers and clinical outcome assessments. We filed a CTA for this trial in April 2019 and plan to conduct the trial at one site in the Netherlands.

The primary objective is to investigate the safety and tolerability of losmapimod for chronic dosing in FSHD patients. The primary endpoints are to assess safety and tolerability over the 52-week period. The secondary endpoints are the change from baseline in pHSP27 and the ratio of pHSP27 to total HSP27 in blood and muscle for assessment of the inhibition of p38a/b during the dosing period. This trial is also designed to provide initial data regarding changes in DUX4-driven gene expression, MRI biomarkers, objective clinical outcome assessments and patient-reported outcomes that may occur at various times following initiation of treatment with losmapimod relative to the pre-treatment period. We intend to use this data to further guide our clinical development strategy for losmapimod in FSHD.

We will measure DUX4-driven gene expression before and during treatment using muscle needle biopsies in affected muscles. All patients will have a pre-treatment biopsy and we will obtain a second muscle needle biopsy from each patient, with half of the patients undergoing a biopsy after four weeks of treatment and the remaining half after approximately 40 weeks of treatment.

We will measure potential losmapimod treatment effects on shoulder and upper arm function and mobility/ambulation, as well as on muscle strength and function and quality of life and activities of daily living, similar to the assessments in the Phase 2b clinical trial. The clinical outcome assessments will be RWS, FSHD-TUG, muscle strength, motor function ability and generic and FSHD-specific patient reports of quality of life and activities of daily living. There will also be an assessment of day-to-day mobility using wearable sensors.

The graphic below presents the design of the Phase 2 open label trial.



Market Research

We engaged Clarion Healthcare, LLC to conduct market research with physicians and payors to better understand the commercial landscape and to assist in our commercial planning. A total of 14 physicians in the United States, European Union and Asia and nine payors and payor experts in the United States and European Union were surveyed. Both groups acknowledged the severity of the disease and lack of any existing therapies for patients. Physicians were asked their views on potentially prescribing a small molecule product candidate that effectively repressed DUX4 gene expression in skeletal muscle and resulted in the preservation of muscle function. Based on an April 2018 report prepared by Clarion, we believe that physicians would be receptive to prescribing a product with these qualities, subject to the efficacy and safety of the product, due to the chronic nature of the disease.

Our Product Candidate for Hemoglobinopathies

Hemoglobinopathies are a category of genetic disorders affecting RBCs. We intend to develop FTX-HbF to elevate the level of fetal hemoglobin for the treatment of patients with certain hemoglobinopathies, namely sickle cell disease and for certain types of b-thalassemia.

Overview of Sickle Cell Disease

Sickle cell disease is a genetic disorder of RBCs. SCD patients typically suffer from serious clinical consequences, which may include vaso-occlusive crises, anemia, pain, infections, stroke, heart disease, pulmonary hypertension, kidney failure, liver disease and reduced life expectancy. According to a study published by the American Medical Association, approximately 32.5% of adult patients with SCD were hospitalized three or more times per year due to pain crises. SCD is reported to shorten patient life expectancy by approximately 20 to 30 years. Patients with SCD are primarily treated by hematologists.

In the United States, where newborn screening for SCD is mandatory, the estimated prevalence is approximately 100,000 individuals. In Europe, the estimated prevalence is approximately 134,000 individuals according to the European Medicines Agency, or EMA. According to the World Health Organization, the global incidence is estimated to be approximately 300,000 births annually. SCD is most prevalent in Africa and the Middle East.

Approved drug treatments for SCD focus primarily on the management and reduction of pain episodes. The two drug treatments approved in the United States are hydroxyurea and L-glutamine.

Hydroxyurea is approved for the treatment of anemia related to SCD to reduce the frequency of painful crises and the need for blood transfusions. Hydroxyurea has a black box warning for myelosuppression and malignancy. In general, it is limited by its adverse side effects, inconsistent patient responses and concerns regarding the cytotoxic effect of the drug. L-glutamine is approved to reduce severe complications associated with the disorder. While treatment with L-glutamine decreases the mean number of pain crises, side effects include nausea, noncardiac chest pain, fatigue, and musculoskeletal pain.

Blood transfusions can be utilized to decrease the sickling of RBCs. While blood transfusions can be critical to manage SCD, there are a number of limitations associated with this therapeutic approach, including limited patient access and serious complications such as iron overload. The only potentially curative treatment currently approved for severe SCD is bone marrow transplantation. However, this treatment option is not commonly used due to the difficulties of finding a suitable matching donor and the risks associated with the treatment, which include an approximately 5% mortality rate. Bone marrow transplantation is more commonly offered to pediatric patients with available sibling-matched donors.

While multiple experimental approaches to treat SCD are being explored in clinical trials, the majority are focused on symptomatic relief or gene therapy approaches. Symptomatic approaches under investigation aim to affect issues associated with cell adhesion, sickling, thrombosis and iron homeostasis. We anticipate that a novel orally available therapy that affects the root cause of SCD may be used in combination with symptomatic therapeutics. Novartis AG, or Novartis, Global Blood Therapeutics, Inc. and GlycoMimetics Inc. in collaboration with Pfizer, Inc. are conducting late stage clinical trials aiming to provide symptomatic relief for patients with SCD. Several gene therapy approaches to treat SCD are focused on elevating fetal hemoglobin, however no gene therapy approaches have been approved for SCD and the efficacy, safety and durability of gene therapy approaches have yet to be established. Gene therapies need to be administered in an in-patient procedure through a bone marrow transplant, which is also referred to as a stem cell transplant or hematopoietic stem cell transplant. As part of the transplant process, the patient receives myeloablative chemotherapy which kills cells in the bone marrow in order to support the gene therapy. Despite ongoing efforts to develop gene therapies for SCD, we believe there is still a high unmet need that could be better addressed by a small molecule, oral therapy to treat the disease by increasing fetal hemoglobin.

SCD Biology

SCD is caused by a mutation in the *HBB* gene. This gene encodes a protein that is a key component of hemoglobin, a protein complex whose function is to transport oxygen in the body. Hemoglobin in adults is a complex of four proteins, two hemoglobin b-subunits and two hemoglobin a-subunits. In patients with SCD, hemoglobin is composed of two mutant b-subunits and two a-subunits and the result is the formation of abnormal hemoglobin. The result of the mutation is less efficient oxygen transport and the formation of RBCs that have a sickle shape. These sickle shaped cells are much less flexible than healthy cells and can block blood vessels (vaso-occlusion) or rupture cells (lysis), leading to pain, anemia, irreversible organ damage or even death.

During fetal development, the major form of hemoglobin is fetal hemoglobin. Similar to hemoglobin in adults, fetal hemoglobin is also a complex of four proteins, two a-subunits and two g-subunits. Shortly after birth, the genes encoding the g-subunits, the *HBG1* and *HBG2* genes, are silenced and the *HBB* gene is activated. As described above, SCD is caused by a mutation in the *HBB* gene that gives rise to mutated b-subunits.

A small subset of individuals with the sickle cell mutation continue to produce high levels of fetal hemoglobin due to inheritance of additional genetic mutations, which is called Hereditary Persistence of Fetal Hemoglobin, or HPFH. The production of fetal hemoglobin in these individuals allows them to maintain at least 30% fetal hemoglobin. Patients with elevated fetal hemoglobin exhibit few, if any, clinical manifestations of SCD. Further, an increase of fetal hemoglobin as low as 3% over baseline in patients

without HPFH, due to either therapeutic intervention or the inheritance of other genetic traits, can result in reduced clinical manifestations of the disease.

Our Approach to Address the Root Cause of SCD

Our strategy to address the root cause of SCD was to identify a drug mechanism that induces expression of fetal hemoglobin. We believe that FTX-HbF may address the root cause of SCD through this mechanism of action.

Overview of b-Thalassemia

b-thalassemia is a rare blood disorder associated with the absence or reduced production of b-globin, which is one of the two proteins that comprise adult hemoglobin. This results in an abnormally low level of hemoglobin as well as an excess of a-globin chains that cause destruction of RBCs. The severity of the phenotype is related to the degree of imbalance between a- and non-a-globin chain synthesis. The absence of b-globin due to *HBB* gene deletions is referred to as b⁰ thalassemia. Other *HBB* gene alterations allow some b-globin to be produced but in reduced amounts. A reduced amount of b-globin is called b⁺thalassemia. Many patients with b-thalassemia require chronic blood transfusions due to severe anemia that results from low hemoglobin levels, which are referred to as transfusion-dependent patients. It is estimated that 40,000 babies are born worldwide with b-thalassemia per year of whom 25,000 require blood transfusions. Patients with b-thalassemia are primarily treated by hematologists.

b-thalassemia has been clinically characterized into three forms, depending on disease severity: major, intermedia and minor. The most severe form, b-thalassemia major (also known as Cooley's anemia), is generally diagnosed shortly after birth and patients have life-threatening anemia. Pediatric patients do not grow and gain weight at the typical rates, and often have liver, heart and bone problems. Many b-thalassemia major patients require frequent blood transfusions to prevent severe anemia, a treatment that itself can cause long-term problems due to a build-up of iron in the body. b-thalassemia intermedia is a less severe form of the disease that results in mild to moderate anemia. These patients sometimes require blood transfusions depending on the severity of the symptoms. Patients with b-thalassemia minor suffer from very mild anemia and generally do not require treatment. Having either b⁰ or b⁺ thalassemia does not necessarily predict clinical disease severity as people with both types have been diagnosed with thalassemia major and thalassemia intermedia. Any increase in fetal hemoglobin has the potential to ameliorate the disease.

The current standard of care for many patients with b-thalassemia is frequent blood transfusions to manage anemia. The only potentially curative therapy for b-thalassemia is allogeneic hematopoietic stem cell transplant, which is associated with risks of complications, including mortality, and is limited to patients with a suitable donor. The European Commission granted conditional marketing authorization for ZYNTGLO, a gene therapy developed by bluebird bio, Inc., or bluebird, for the treatment of adult and adolescent patients with transfusion-dependent b-thalassemia and with certain genotypes, in Europe in June 2019. bluebird announced that it plans to file a biologics license application, or BLA, in the United States in 2019. Acceleron Pharma, Inc., or Acceleron, in collaboration with Celgene Corp., or Celgene, is conducting Phase 3 clinical trials of luspatercept (ACE-536), an erythroid maturation agent. Celgene submitted a BLA for luspatercept for the treatment of adult patients with anemia associated with b-thalassemia and who require frequent transfusions. Celgene and Acceleron submitted a marketing authorization application to the EMA in the second quarter of 2019. There are also multiple other experimental approaches to treat b-thalassemia being explored in clinical trials, including approaches that use small molecule, gene therapy and gene editing approaches. Despite ongoing efforts to develop new therapies for b-thalassemia, we believe there is still a high unmet need that could be addressed by a small molecule, oral therapy to treatment the disease by increasing fetal hemoglobin.

Biology of β -Thalassemia

β -thalassemia is caused by genetic mutations in the *HBB* gene. The mutations interfere with the production of β -globin. Some mutations result in no β -globin being produced, while other mutations result in a decreased amount of β -globin being produced.

Our Approach to Address the Root Cause of β -Thalassemia

We believe that some types of β -thalassemia may be treated by a therapy that upregulates fetal hemoglobin. Babies born with β -thalassemia major generally do not have any symptoms shortly after birth because they have fetal hemoglobin in their blood. As the fetal hemoglobin levels decrease after birth and the β -globin fails to increase, anemia appears and the babies with β -thalassemia begin to exhibit symptoms of the disease. Patients with β -thalassemia intermedia that have higher levels of fetal hemoglobin have fewer symptoms than patients with low levels of fetal hemoglobin. We believe that FTX-HbF may be suitable for clinical development for the treatment of patients who are not β^0 but who are transfusion dependent.

Our Product Engine Identified the Drug Target for SCD and β -Thalassemia

Applying our product engine, we conducted target identification and validation activities using human umbilical cord blood-derived erythroid progenitor 2, or HUDEP2, cells as a model to study fetal hemoglobin reactivation. HUDEP2 cells are immature RBCs. By screening our small molecule probe library and a CRISPR library, we identified several potential drug targets that activated the *HBG1/2* genes and resulted in fetal hemoglobin elevation. Each screening approach identified the same protein complex which we believe plays an important role in the expression of genes responsible for the production of fetal hemoglobin. We conducted additional validation experiments in which we observed that inhibition of several components of this complex resulted in the desired elevation of fetal hemoglobin. We also observed that inhibition of these components did not adversely affect important cell health markers.

We selected a member of this protein complex for drug discovery activities following an assessment of its tractability as a drug target, which we refer to as the HbF drug target. The normal physiological role of the HbF drug target is to facilitate a post-translational protein modification, and the goal of our medicinal chemistry program was to optimize inhibitors of the HbF drug target. We developed *in vitro* and *in vivo* target engagement assays, as well as enabled X-ray crystallography, to discover and develop FTX-HbF, a novel small molecule inhibitor of the HbF drug target.

FTX-HbF

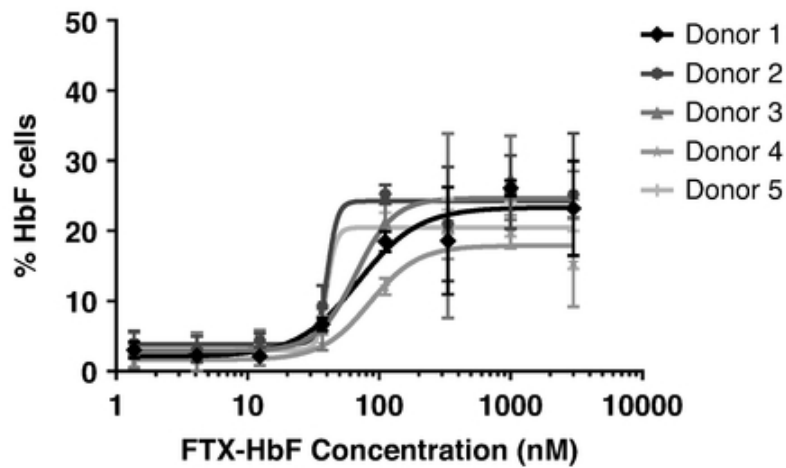
FTX-HbF, our novel small molecule that we designed to inhibit the HbF drug target and thereby elevate fetal hemoglobin, possesses properties that we believe are well aligned with preferred parameters for oral drug delivery. We studied the cellular potency and the PK data of FTX-HbF in preclinical animal models and observed that its profile would be predictive of once or twice daily oral administration. We have not observed any off-target concerns in our *in vitro* profiling studies, and we are conducting *in vivo* toxicology studies to evaluate FTX-HbF. We have initiated IND-enabling activities and we aim to submit an IND in mid-2020.

Preclinical Studies

We have observed *in vitro* and *in vivo* activation of the *HBG1/2* genes in preclinical studies with FTX-HbF. We observed that FTX-HbF elevated levels of fetal hemoglobin with minimal adverse effect on important cellular health markers. As depicted in the graphic below, we also observed *in vitro* upregulation of fetal hemoglobin in primary human CD34+ cells differentiated into RBCs from five different human

donors after five days of drug treatment. FTX-HbF showed a significant elevation of fetal hemoglobin over baseline in each of these five cell lines.

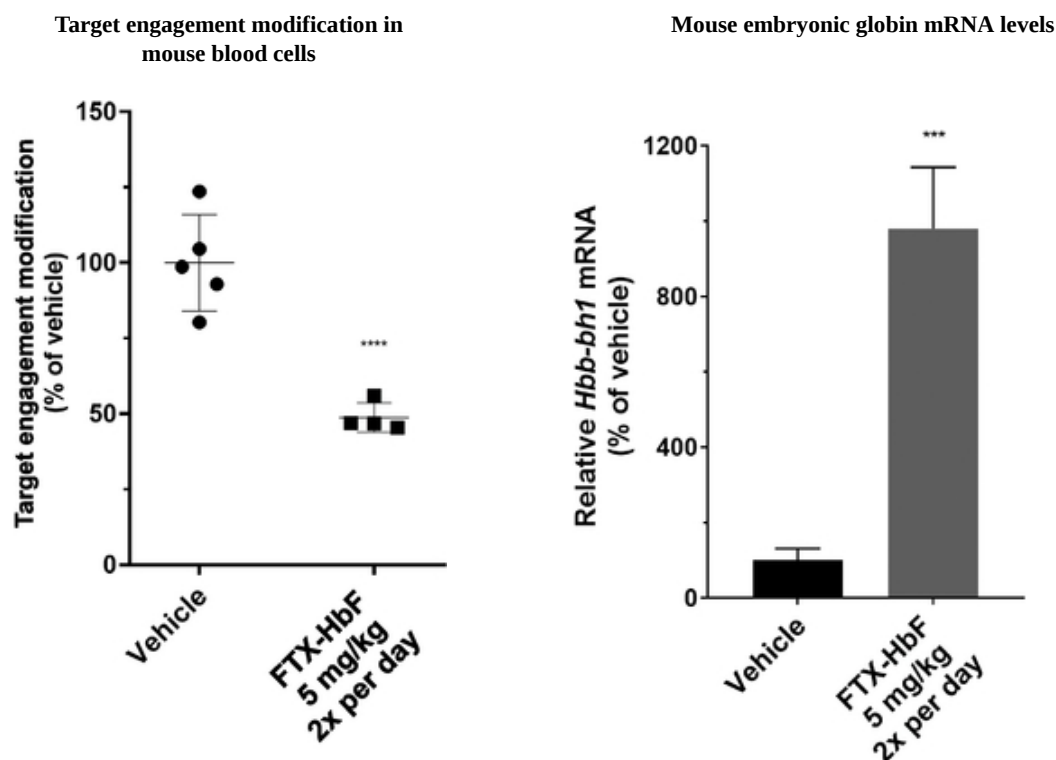
**Effect of FTX-HbF treatment
in differentiated primary human CD34+ cells**



Additionally, we compared the effect of FTX-HbF in CD34+ derived cells relative to that of hydroxyurea. We observed that hydroxyurea had a minimal impact on fetal hemoglobin elevation, whereas we observed that FTX-HbF significantly elevated fetal hemoglobin. In cells treated with the combination of FTX-HbF and hydroxyurea, we observed an increased effect relative to either compound alone.

In preclinical PK/PD studies in mice, we observed that blood cells had dose-dependent drug target engagement after 4.5 days of oral treatment. We believe our drug target is conserved between species, which is supported by our observation of a concomitant upregulation of the mouse embryonic globin gene under conditions where we observed drug target engagement. Since mice do not have the *HBG1/2* genes found in humans, we used the mouse embryonic globin gene *hbb-bh1* as a surrogate for the human *HBG1/2* genes. We measured the target engagement in the mouse from whole blood. We concluded from the data

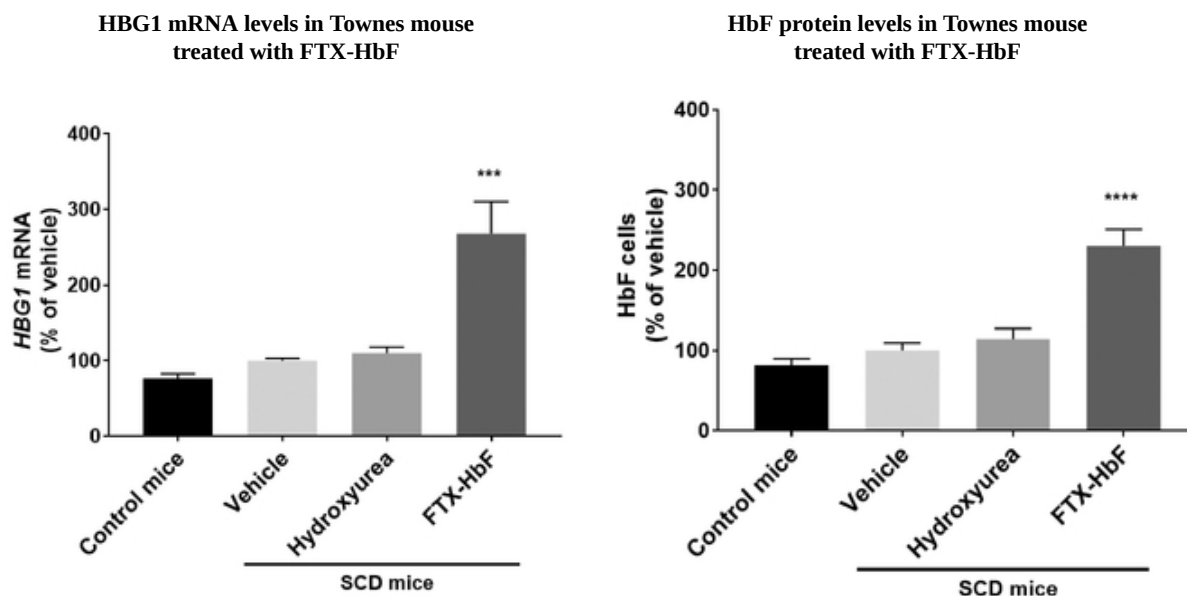
that FTX-HbF engaged the drug target *in vivo* and modulated the endogenous mouse globin gene expression program. The results of this study are depicted below.



In the graphic on the left, we measured the amount of drug target engagement modification in mouse blood cells after five days of treatment. In the vehicle-treated mice, we observed maximum levels of protein modification, whereas in the FTX-HbF treated mice, we observed significantly lower levels of modification, which indicates significant target engagement. Each point represents the value for a different mouse, shown as a percent of the average vehicle-treated value. In the graphic on the right, we determined the level of mouse embryonic globin mRNA levels in mouse blood after five days of treatment. The data is from an average of four or five mice per treatment. In these studies, we used a conventional method of assessing statistical significance known as a two-tailed test. The p-value for each of the studies depicted above was 0.0005. A p-value is a conventional statistical method for measuring the statistical significance of experimental results. A p-value of less than 0.05 is generally considered to represent statistical significance, meaning that there is a less than five percent likelihood that the observed results occurred by chance.

Additionally, we studied FTX-HbF in a mouse model of SCD, known as the Townes mouse model. In this model, mouse globin genes have been replaced with human globin genes, thereby allowing investigations of mechanisms that may regulate human hemoglobin gene expression. The Townes mouse model has been widely used to study potential treatments for SCD. As shown in the figures below, we observed that FTX-HbF resulted in a significant increase in *HBG1* gene expression and HbF protein after

28 days of dosing at 5 mg/kg twice per day. Hydroxyurea did not result in a significant elevation of *HBG1* gene expression.



In the graphic on the left, we determined the level of human HbG1 mRNA for the four treatment conditions from mouse blood, shown as a percentage of vehicle-alone-treated SCD mice. In the graphic on the right, we determined the level of human HbF protein for the four treatment conditions, shown as a percentage of vehicle-alone-treated SCD mice. Each value represents the mean value from five or six mice per treatment after 28 days of treatment. In these studies, we used a conventional method of assessing statistical significance known as a one-way analysis of variance, or ANOVA. The p-value for the study depicted on the left was less than 0.0001 and the p-value for the study depicted on the right was less than 0.001.

Our Development Plan for FTX-HbF

We are currently conducting IND-enabling studies and intend to submit an IND for FTX-HbF in mid-2020. We intend to initiate a Phase 1 clinical trial of FTX-HbF in healthy volunteers in late 2020. The Phase 1 trial will be designed to investigate the safety and tolerability of single and multiple ascending doses of FTX-HbF and to define the relationship between PK and target engagement in blood.

Following completion of the Phase 1 trial, we would consider a parallel development path in SCD and b-thalassemia. We expect that our target SCD patient population will be adult SCD patients with inadequate disease control and that concomitant use of hydroxyurea and/or L-glutamine will be allowed when available. We expect that our target b-thalassemia patient population will be adult b-thalassemia patients who are not b⁰ but are transfusion-dependent.

Discovery Screening Programs

We have leveraged our proprietary product engine to discover targets that we are pursuing with small molecules for FSHD and SCD and b-thalassemia. We are leveraging the broad applicability of our product engine to discover drug targets for other rare, genetically defined diseases across neuromuscular and CNS diseases. We plan to complete four additional screens in 2019. These four diseases and our approach to identifying targets to address the root cause of each disease are further described below.

DISCOVERY SCREENING INDICATIONS	DIRECTION OF GENE MODULATION	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	STATUS
Duchenne Muscular Dystrophy	UTRN ↑	▶					Target ID / Validation
Friedreich Ataxia	FXN ↑	▶					Target ID / Validation
Myotonic Dystrophy 1	DMPK ↓	▶					Target ID / Validation
α-Synucleinopathies	SCNA ↓	▶					Target ID / Validation

We currently plan to conduct six additional screens in 2020, and we are undergoing a rigorous disease assessment and selection process. Although we believe our product engine and screening efforts are robust and have a high likelihood of identifying drug targets for each new screen area, we intend to focus on advancing the most attractive targets and development candidates identified from our screening efforts for development. We may also selectively consider external partnerships for those areas that may be more appropriate for a partner to advance.

Duchenne Muscular Dystrophy

Duchenne muscular dystrophy, or DMD, is the most common childhood-onset muscular dystrophy with a prevalence of approximately one out of every 3,500 male births. Patients usually are diagnosed before five years of age and typically require the use of wheelchairs before their teens. Life-threatening cardiac and respiratory complications result in a life expectancy of 20-30 years without any treatment. Currently, management of these complications by standard of care treatment (*e.g.*, corticosteroids) can extend life expectancy, however, there are no approved disease-modifying therapies. This X-chromosome linked disease is caused by mutations in the *DMD* gene resulting in the loss of expression or function of the protein dystrophin. Dystrophin is an integral component of a large multiprotein complex that functions by linking the sarcolemma (the plasma membrane in muscle fibers) with the cytoskeleton and other motor machinery. In the absence of dystrophin, progressive muscle fiber degeneration results in loss of function and clinical manifestation of the disease.

Our goal is to apply our product engine to identify drug targets to increase the expression of utrophin, a dystrophin-related protein, that can replace the function of dystrophin in the membrane and address the dysfunction due to damaged muscle fibers. Utrophin is normally expressed in other tissues and studies have shown that higher levels of this protein result in functional improvements in animal models of the disease.

Friedreich Ataxia

Friedreich ataxia, or FA, a neuromuscular disorder affecting about one out of every 40,000 people, is the most common hereditary ataxia, with a typical age of onset between 10 and 15 years. The progressive impaired muscle coordination, ataxia, is caused by the degeneration of neurons in the cerebellum and dorsal root ganglia in the spinal cord. FA patients also commonly suffer from life-threatening heart conditions such as hypertrophic cardiomyopathy, myocardial fibrosis and heart failure. There are no approved disease-modifying therapies. The genetic root cause of FA is an expansion of a sequence in the frataxin gene, *FXN*, which causes its downregulation. Loss of function of frataxin, an important protein involved in iron metabolism, results in oxidative stress and mitochondrial dysfunction.

Our goal is to apply our product engine to identify drug targets that can upregulate the levels of frataxin protein to levels that will impact and restore function to prevent neuronal and cardiac cell degeneration.

Myotonic Dystrophy 1

Myotonic dystrophy 1, or DM1, is the most common adult-onset muscular dystrophy affecting about one out of every 8,000 people, with a typical age of onset between 20 and 40 years. It is characterized by muscle weakness and myotonia. Cardiopulmonary complications when present can be life-threatening and current treatments are directed toward managing these complications. There are no approved disease-modifying therapies. DM1 is caused by expansion of a triple nucleotide repeat present in the non-coding region of the *DMPK* gene and are part of its mature transcript. More than 50 cytosine-thymine-guanine repeats are usually associated with pathology and disease severity is proportional to the number of repeats, which can expand to over 4,000. The accumulation of *DMPK* gene transcripts containing long repeats result in the sequestration of proteins important for the correct splicing of important transcripts participating in the function of skeletal and cardiac muscle and other tissues.

Our goal is to apply our product engine to identify drug targets that may lead to downregulation of the expression of the *DMPK* gene in order to reduce the levels of the pathological repeats and improve muscle function. Reduction of *DMPK* gene expression in DM1 models has been shown to reduce aberrant splicing and to be well tolerated.

***α*-Synucleinopathies**

In rare cases, *α*-Synucleinopathies result from point mutations and multiplications in the *SNCA* gene that encodes the protein *α*-synuclein. Familial forms of Parkinson's disease can result from these mutations and multiplications in the *SNCA* gene. Parkinson's disease is a common progressive neurodegenerative disease characterized by movement disorders such as bradykinesia, rigidity and tremor. Genome wide association studies have linked single nucleotide polymorphisms in *SNCA* with increased risk of Parkinson's disease. These mutations have been shown to increase levels of pathological, aggregated *α*-synuclein, leading to the loss of midbrain dopaminergic neurons important for motor control. Abnormal deposits of *α*-synuclein protein, or Lewy bodies, are the characteristic histological signature of Parkinson's disease at autopsy. According to the Parkinson's Foundation, nearly one million people will be living with Parkinson's disease in the United States by 2020.

Our goal is to use our product engine to identify drug targets for genetically defined *α*-synucleinopathies that may lead to reduction in *α*-synuclein levels in the most relevant cell type for Parkinson's disease—dopaminergic neurons. Our goal is to lower the overall *α*-synuclein load in the brain of patients with sporadic or genetic *α*-synucleinopathies by starting treatment early in their disease course to prevent further *α*-synuclein-dependent neurodegeneration, thus representing a potential disease-modifying approach across all *α*-synucleinopathies.

Right of Reference and License Agreement with GlaxoSmithKline

In February 2019, we entered into a right of reference and license agreement with affiliates of GSK, pursuant to which GSK granted us a right of reference to certain INDs filed with the FDA and controlled by GSK or its affiliates relating to losmapimod and an exclusive worldwide license under certain patent rights related to losmapimod. The agreement also provides us with an exclusive worldwide license to certain of GSK's preclinical and clinical data with respect to losmapimod. As partial consideration for the right of reference and licenses granted under the agreement, we issued 12,500,000 shares of our Series B preferred stock to GSK at the time we entered into the reference and license agreement. The agreement obligates us to use commercially reasonable efforts to develop and commercialize a licensed product for the treatment of FSHD.

The agreement grants us an exclusive, sublicensable license under the licensed patent rights and data rights to research, develop and commercialize losmapimod or any product containing losmapimod as an API, which we refer to as a licensed product, to treat disease in humans. GSK retained the right, without the right to grant sublicenses, to conduct nonclinical research under the licensed patents and data rights and, with our consent, GSK may engage in certain developmental activities relating to the use of a licensed product in connection with a specified prophylactic use. GSK also agreed to and has since transferred to us its existing manufactured supply of losmapimod.

Under the agreement, we will be obligated to make milestone payments to GSK aggregating up to \$37.5 million upon the achievement of specified clinical and regulatory milestones with respect to the first licensed product to achieve such milestones, and up to \$60.0 million upon the achievement of one-time aggregate annual worldwide net sales milestones. We will also be obligated to pay royalties ranging from a mid single-digit percentage to a low double-digit, but less than teens, percentage to GSK based on our, and any of our affiliates' and sublicensees', annual net sales of licensed products. The royalties are payable on a product-by-product and country-by-country basis, and may be reduced in specified circumstances.

Our obligation to make royalty payments extends with respect to a licensed product in a country until the earlier of the approval of a generic version of such licensed product by the applicable regulatory agency

in such country or the tenth anniversary of the first commercial sale of such licensed product in such country, which we refer to as the royalty term. Following the expiration of any exclusive marketing rights or data exclusivity rights granted by a regulatory authority, other than patent rights, for any licensed product on a country-by-country basis, the applicable royalty rate will be reduced. Additionally, if we or our affiliates or sublicensees determine that it is necessary to obtain a license from a third party under any patent rights to exploit a licensed product in a country, then we may deduct a certain percentage of the license fees under such third party license payable by us to the third party from the royalty payment that would otherwise be due to GSK in such country.

If, prior to our completion of the first Phase 2 clinical trial for a licensed product, we wish to sublicense any of the licensed patent or data rights granted to us under the agreement to any third party outside of the United States, we must notify GSK of the terms on which we propose to grant such sublicense. GSK has the right to enter into negotiations with us for such sublicense, and if GSK so elects, then we must negotiate in good faith with GSK for a prescribed period. If we and GSK do not agree to a sublicense of the relevant rights, we may sublicense the relevant rights to the third party on terms no less favorable than any terms offered to us by GSK.

The agreement continues on a country-by-country and licensed product-by-licensed product basis until the expiration of the royalty term in each country, at which time the agreement expires with respect to such licensed product in such country and we shall have a fully-paid up, royalty-free and perpetual license to the licensed patent rights and data with respect to such licensed product in such country. Either party has the right to terminate the agreement if the other party has materially breached in the performance of its obligations under the agreement and such breach has not been cured within the applicable cure period.

We also agreed to provide GSK the opportunity to purchase shares of common stock in connection with this offering equal to the proportion that the shares of common stock held by GSK (assuming conversion of all preferred stock into common stock upon consummation of this offering) bear to the total number of shares of common stock immediately prior to the closing of this offering (assuming conversion of all preferred stock into common stock upon consummation of this offering and all outstanding options). If GSK exercises its rights to purchase shares of common stock in connection with this offering, subject to certain conditions, GSK may purchase shares offered in this offering or may purchase shares of common stock in a private placement that is expected to close concurrently with this offering, in each case at the initial per share public offering price.

Intellectual Property

We strive to protect and enhance the proprietary technology, inventions and improvements that are commercially important to the development of our business, including by seeking, maintaining and defending patent rights, whether developed internally or licensed from third parties. We also rely on trade secrets, know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen and maintain our proprietary position in our field.

Our future commercial success depends, in part, on our ability to: obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business; defend and enforce in our intellectual property rights, in particular our patents rights; preserve the confidentiality of our trade secrets; and operate without infringing, misappropriating or violating the valid and enforceable patents and proprietary rights of third parties. Our ability to stop third parties from making, using, selling, offering to sell or importing our products may depend on the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities.

The patent positions of biotechnology and pharmaceutical companies like ours are generally uncertain and can involve complex legal, scientific and factual issues. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient proprietary protection from competitors. We also cannot ensure that patents will issue with respect to any patent applications that we or our licensors may

file in the future, nor can we ensure that any of our owned or licensed patents or future patents will be commercially useful in protecting our product candidates and methods of manufacturing the same. In addition, the coverage claimed in a patent application may be significantly reduced before a patent is issued, and its scope can be reinterpreted and even challenged after issuance. As a result, we cannot guarantee that any of our products will be protected or remain protectable by enforceable patents. Moreover, any patents that we hold may be challenged, circumvented or invalidated by third parties. See "Risk Factors—Risks Related to Our Intellectual Property" for a more comprehensive description of risks related to our intellectual property.

We generally file patent applications directed to our key programs in an effort to secure our intellectual property positions vis-a-vis these programs. As of June 15, 2019, we owned one allowed U.S. patent application, one U.S. pending non-provisional patent application, four foreign pending patent applications, three pending Patent Cooperation Treaty, or PCT, applications and four U.S. provisional patent applications.

The intellectual property portfolio for our most advanced programs as of June 15, 2019, is summarized below. Prosecution is a lengthy process, during which the scope of the claims initially submitted for examination by the U.S. Patent and Trademark Office may be significantly narrowed before issuance, if issued at all. We expect this may be the case with respect to some of our pending patent applications referred to below.

Losmapimod and Derivatives

The patent portfolio for losmapimod is based upon Fulcrum-owned patent applications and in-licensed patents directed to new methods of using losmapimod and other p38 inhibitors to treat FSHD, pharmaceutical compositions generically and specifically covering p38 inhibitors, and methods for identifying novel compositions to treat FSHD. As of June 15, 2019, we owned one allowed U.S. patent application, one U.S. pending non-provisional patent application, four foreign patent applications filed in Taiwan, Uruguay, Venezuela and Argentina and three pending PCT applications relating to our p38a/b program, primarily relating to methods of using losmapimod and certain other p38 inhibitors for the treatment of FSHD. On June 19, 2019, we were notified by the USPTO that a patent covering the use of losmapimod for the treatment of patients with FSHD will issue to us on July 9, 2019. We own the patent application relating to this patent and, once issued, we will own the patent. While we believe that the specific and generic claims contained in our allowed U.S. patent application provide protection for the method of using losmapimod for the treatment of FSHD, and is not implicated by invalidating prior art, third parties may nevertheless challenge such claims. If any such claims are invalidated or rendered unenforceable for any reason, we will lose valuable intellectual property rights and our ability to prevent others from competing with us would be impaired. Any U.S. or ex-U.S. patents that may issue from pending applications that we own, if any, for our p38a/b program are projected to have a statutory expiration date in 2038, excluding any additional term for patent term adjustments or patent term extension, if applicable.

Losmapimod is currently protected by patents owned by GSK (as a composition of matter and certain uses which do not include FSHD) and certain of these patents are licensed to us. As soon as the patents covering the composition of matter expire on February 10, 2023, or are no longer in-force, the GSK-licensed patents will no longer be a barrier to entry for any unclaimed new uses, including FSHD. Even during the term of these composition of matter patents, losmapimod can still be developed in the meantime in certain geographies, including in the United States, under safe harbor regulations.

FTX-HbF

As of June 15, 2019, the intellectual property portfolio for our FTX-HbF program includes one U.S. provisional patent application directed to pharmaceutical compositions generically and specifically covering inhibitors of a certain protein or protein complex that regulate fetal hemoglobin, as well as to

methods for using and making these compositions. In order to continue to pursue protection based on this provisional patent application, we will need to file a PCT, foreign applications, and/or U.S. non-provisional patent application prior to the applicable deadline. If we do continue to pursue protection, any patents that may issue from the non-provisional patent applications would be projected to have statutory expiration dates in 2039, excluding any additional term for patent term adjustments or patent term extension, if applicable. While we believe that the specific and generic claims, contained in our U.S. provisional patent application, if filed as U.S. non-provisional application, PCT application and/or foreign application(s), provide protection for the claimed pharmaceutical compositions and methods of use and are not implicated by invalidating prior art, third parties may nevertheless challenge such claims. If any such claims are invalidated or rendered unenforceable for any reason, we will lose valuable intellectual property rights and our ability to prevent others from competing with us would be impaired.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application.

In the United States, the term of a patent covering an FDA-approved drug may, in certain cases, be eligible for a patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984 as compensation for the loss of patent term during the FDA regulatory review process. The period of extension may be up to five years, but cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval. Only one patent among those eligible for an extension and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Similar provisions are available in Europe and in certain other jurisdictions to extend the term of a patent that covers an approved drug. It is possible that issued U.S. patents covering the use of losmapimod and products from our intellectual property may be entitled to patent term extensions. If our use of drug candidates or the drug candidate itself receive FDA approval, we intend to apply for patent term extensions, if available, to extend the term of patents that cover the approved use or drug candidate. We also intend to seek patent term extensions in any jurisdictions where available, however, there is no guarantee that the applicable authorities, including the FDA, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions.

In addition to patent protection, we rely upon unpatented trade secrets and confidential know-how and continuing technological innovation to develop and maintain our competitive position. However, trade secrets and confidential know-how are difficult to protect. We seek to protect our proprietary information, in part, using confidentiality agreements with any collaborators, scientific advisors, employees and consultants and invention assignment agreements with our employees. We also have agreements requiring assignment of inventions with selected consultants, scientific advisors and collaborators. These agreements may not provide meaningful protection. These agreements may also be breached, and we may not have an adequate remedy for any such breach. In addition, our trade secrets and/or confidential know-how may become known or be independently developed by a third party, or misused by any collaborator to whom we disclose such information. Despite any measures taken to protect our intellectual property, unauthorized parties may attempt to copy aspects of our products or to obtain or use information that we regard as proprietary. Although we take steps to protect our proprietary information, third parties may independently develop the same or similar proprietary information or may otherwise gain access to our proprietary information. As a result, we may be unable to meaningfully protect our trade secrets and proprietary information. See "Risk Factors—Risks Related to our Intellectual Property" for a more comprehensive description of risks related to our intellectual property.

Manufacturing

We do not have any manufacturing facilities. We obtained sufficient losmapimod tablets, or drug product, from GSK to complete our planned Phase 2 clinical trials. We obtained losmapimod API from GSK and plan to engage a contract manufacturing organization to convert the API into losmapimod

tablets. We believe that the quantity of API will be sufficient to complete further clinical trials in FSHD. We believe that we have all the necessary information from GSK to enable the required technology transfers to contract manufacturing organizations. We also intend to identify and engage contract manufacturing organizations to prepare our own API and to manufacture tablets to support potential commercialization.

We expect to rely on third parties for the manufacture of FTX-HbF and any future product candidates for preclinical and clinical testing, as well as for commercial manufacture if our product candidates receive marketing approval. Our lead product candidates are small molecules and can be manufactured in reliable and reproducible synthetic processes from readily available starting materials. We expect to continue to develop product candidates that can be produced cost-effectively at contract manufacturing facilities.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technologies, knowledge, experience and scientific resources provide us with competitive advantages, we face competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industry may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

The key competitive factors affecting the success of all of our therapeutic product candidates, if approved, are likely to be their efficacy, safety, convenience, price, the effectiveness of companion diagnostics in guiding the use of related therapeutics, the level of generic competition and the availability of reimbursement from government and other third-party payors.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products. If our product candidates achieve marketing approval, we expect that they will be priced at a significant premium over competitive generic products.

If our lead product candidates are approved for the indications for which we are currently undertaking clinical trials, they will compete with the therapies and currently marketed drugs discussed below.

FSHD

There are no approved therapies for the treatment of FSHD. Controlled trials of albuterol, corticosteroids and a myostatin inhibitor all failed to demonstrate a clinical benefit to patients with FSHD. Low-intensity aerobic exercise tailored to the patient's distribution of weakness may provide some limited

beneficial effect. Limited range of motion in the shoulder girdle can stem from periscapular muscle weakness, and in such cases surgical scapular fixation can result in some functional improvement for certain patients. There is also no standard practice regarding the use of physical or occupational therapy across countries and sites.

We are not aware of any product candidate currently in clinical development for FSHD with the same mechanism of action as losmapimod or that is designed to treat the root cause of FSHD. We are aware of ACE-083, a locally injected myostatin inhibitor for intermittent treatment of weakness for ankle dorsiflexion (foot drop) and elbow flexion, which is currently in Phase 2a clinical development for FSHD by Acceleron. aTyr Pharma, Inc., or aTyr, conducted a Phase 1/2 clinical trial of resolaris, a physiocrine immune modulation protein. aTyr discontinued development of resolaris in FSHD. aTyr publicly disclosed that they do not intend to further develop resolaris without a partner.

SCD

Approved drug treatments for SCD focus primarily on the management and reduction of pain episodes. The two drug treatments approved in the United States are hydroxyurea and L-glutamine. Hydroxyurea, marketed by Bristol-Myers Squibb Company, is approved for the treatment of anemia related to SCD, to reduce the frequency of painful crises and the need for blood transfusions. L-glutamine, marketed by Emmaus Life Sciences, Inc., is approved to reduce severe complications associated with the disorder.

Blood transfusions can be utilized to decrease the sickling of RBCs. While blood transfusions can be critically important to the management of SCD, there are a number of limitations associated with this therapeutic approach, including limited patient access and serious complications such as iron overload. The only potentially curative treatment currently approved for severe SCD is bone marrow transplantation. However, this treatment option is not commonly used given the difficulties of finding a suitable matched donor and the risks associated with the treatment, which include an approximately 5% mortality rate. Bone marrow transplantation is more commonly offered to pediatric patients with available sibling-matched donors.

FTX-HbF could face competition from a number of different therapeutic approaches in development for patients with SCD. Novartis is conducting Phase 3 clinical trials of crizanlizumab, an anti-P-selectin monoclonal antibody, for the prevention of vaso-occlusive crises in patients with SCD. In January 2019, Novartis announced that crizanlizumab was granted breakthrough therapy designation by the FDA, and that Novartis expects to file a BLA for crizanlizumab in the first half of 2019. Global Blood Therapeutics, Inc. is conducting a Phase 3 clinical trial of voxelotor (GBT440), a hemoglobin modifier, to prevent the sickling of RBCs. GlycoMimetics Inc. and Pfizer, Inc. are conducting a Phase 3 clinical trial of rivipansel (GMI-1070), a pan-selectin inhibitor. bluebird has been granted conditional marketing authorization by the European Commission for ZYNTEGLO, a gene therapy, as a one-time treatment for SCD that aims to treat SCD by inserting a functional human b-globin gene into the patient's own hematopoietic stem cells *ex vivo* and then transplanting the modified stem cell into the patient's bloodstream. EpiDestiny, Inc., or EpiDestiny, in collaboration with Novo Nordisk A/S, is evaluating EPI01, a small molecule designed to increase production of fetal hemoglobin, in Phase 2 clinical trials. Imara, Inc. is evaluating IMR-687, a PDE9 inhibitor, in a Phase 2a clinical trial in patients with sickle cell anemia. Aruvant Sciences, Inc. is evaluating RVT-1801, a gene therapy, in a Phase 1/2 trial. Sangamo Therapeutics Inc., or Sangamo, in collaboration with Bioverativ Inc., or Bioverativ, is developing BIVV-003, a gene editing cell therapy that modifies cells to produce functional RBCs using fetal hemoglobin. There are also several other gene editing approaches being evaluated by Intellia Therapeutics, Inc. (in collaboration with Novartis), Editas Medicine, Inc. and CRISPR Therapeutics AG (in collaboration with Vertex Pharmaceuticals Incorporated, or Vertex). Pfizer conducted a Phase 1b clinical trial with PF-04447943, a PDE9 inhibitor, in patients with SCD.

***b*-thalassemia**

The current standard of care for many patients with *b*-thalassemia is frequent blood transfusions to manage anemia. The only potentially curative therapy for *b*-thalassemia is allogeneic hematopoietic stem cell transplant, which is associated with serious risk and is limited to patients with a suitable donor. The European Commission granted conditional marketing authorization for ZYNTEGLO, a gene therapy developed by bluebird for the treatment of adult and adolescent patients with transfusion-dependent *b*-thalassemia and with certain genotypes, in Europe in June 2019. bluebird announced that it plans to file a BLA in the United States in 2019.

FTX-HbF could face competition from a number of different therapeutic approaches are in development as a therapeutic option for patients with transfusion-dependent *b*-thalassemia. Acceleron, in collaboration with Celgene, is conducting Phase 3 clinical trials of luspatercept (ACE-536), an erythroid maturation agent. Celgene submitted a BLA for luspatercept for the treatment of adult patients with anemia associated with *b*-thalassemia and who require frequent transfusions. Celgene and Acceleron submitted a marketing authorization application, or MAA, to the EMA in the second quarter of 2019.

Bellicum Pharmaceuticals, Inc. is conducting a Phase 1/2 clinical trial to evaluate a modified donor T cell therapy to be used in conjunction with hematopoietic stem cell transplant. Kiadis Pharma is conducting Phase 2 and Phase 3 clinical trials of an adjunctive T cell immunotherapy treatment in conjunction with hematopoietic stem cell transplant. EpiDestiny, in collaboration with Novo Nordisk A/S, is evaluating EPI01, a small molecule designed to increase production of fetal hemoglobin, in Phase 2 clinical trials. Orchard Therapeutics plc is conducting Phase 2 clinical trials of OTL-300, an autologous *ex vivo* gene therapy for the treatment of transfusion-dependent *b*-thalassemia. Sangamo, in collaboration with Bioverativ, is conducting a Phase 1/2 clinical trial of ST-400, which uses a genome-edited cell therapy approach designed to produce functional RBCs using fetal hemoglobin. CRISPR Therapeutics AG, in collaboration with Vertex, is conducting a Phase 1/2 clinical trial of CTX001, which uses a gene editing approach to upregulate the expression of fetal hemoglobin, in patients with transfusion-dependent *b*-thalassemia.

Government Regulation and Product Approvals

Government authorities in the United States at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, pricing, reimbursement, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of biopharmaceutical products. The processes for obtaining marketing approvals in the United States and in foreign countries and jurisdictions, along with compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

Approval and Regulation of Drugs in the United States

In the United States, drug products are regulated under the Federal Food, Drug and Cosmetic Act, or FDCA, and applicable implementing regulations and guidance. The failure of an applicant to comply with the applicable regulatory requirements at any time during the product development process, including non-clinical testing, clinical testing, the approval process or post-approval process, may result in delays to the conduct of a study, regulatory review and approval and/or administrative or judicial sanctions. These sanctions may include, but are not limited to, the FDA's refusal to allow an applicant to proceed with clinical trials, refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, adverse publicity, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits or civil or criminal investigations and penalties brought by the FDA or Department of Justice, or DOJ, or other government entities, including state agencies.

An applicant seeking approval to market and distribute a new drug in the United States generally must satisfactorily complete each of the following steps before the product candidate will be approved by the FDA:

- preclinical testing including laboratory tests, animal studies and formulation studies, which must be performed in accordance with the FDA's good laboratory practice, or GLP, regulations and standards;
- submission to the FDA of an IND for human clinical testing, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials to establish the safety, potency and purity of the product candidate for each proposed indication, in accordance with current good clinical practices, or GCP;
- preparation and submission to the FDA of a new drug application, or NDA, for a drug product which includes not only the results of the clinical trials, but also, detailed information on the chemistry, manufacture and quality controls for the product candidate and proposed labelling for one or more proposed indication(s);
- review of the product candidate by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities, including those of third parties, at which the product candidate or components thereof are manufactured to assess compliance with current good manufacturing practices, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of any FDA audits of the non-clinical and clinical trial sites to assure compliance with GCP and the integrity of clinical data in support of the NDA;
- payment of user fees and securing FDA approval of the NDA to allow marketing of the new drug product; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct any post-approval studies required by the FDA.

Preclinical Studies

Before an applicant begins testing a product candidate with potential therapeutic value in humans, the product candidate enters the preclinical testing stage, including *in vitro* and animal studies to assess the safety and activity of the drug for initial testing in humans and to establish a rationale for therapeutic use. Preclinical tests include laboratory evaluations of product chemistry, formulation and stability, as well as other studies to evaluate, among other things, the toxicity of the product candidate. The conduct of the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements, including GLP regulations and standards. The results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity and long-term toxicity studies may continue after the IND is submitted.

The IND and IRB Processes

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other

things, the requirement that all research subjects provide their voluntary informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND.

An IND is an exemption from the FDCA that allows an unapproved product candidate to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer such investigational product to humans. Such authorization must be secured prior to interstate shipment and administration of any product candidate that is not the subject of an approved NDA. In support of a request for an IND, applicants must submit a protocol for each clinical trial, and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, must be submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the filing of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research subjects will be exposed to unreasonable health risks. At any time during this 30-day period or thereafter, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold or partial clinical hold. In these cases, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin.

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial. Clinical holds are imposed by the FDA whenever there is concern for patient safety and may be a result of new data, findings, or developments in clinical, nonclinical, and/or chemistry, manufacturing, and controls. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. For example, a specific protocol or part of a protocol may not be allowed to proceed, while other protocols may be allowed. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a clinical hold or partial clinical hold, a clinical trial may only resume after the FDA has so notified the sponsor. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the clinical trial can proceed.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all FDA IND requirements must be met unless waived. When a foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA in order to use the study as support for an IND or application for marketing approval. Specifically, on April 28, 2008, the FDA amended its regulations governing the acceptance of foreign clinical studies not conducted under an investigational new drug application as support for an IND or a new drug application. The final rule provides that such studies must be conducted in accordance with GCP, including review and approval by an independent ethics committee, or IEC, and informed consent from subjects. The GCP requirements in the final rule encompass both ethical and data integrity standards for clinical studies. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

In addition to the foregoing IND requirements, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. An IRB can

suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee. This group provides authorization as to whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the study. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed to an unacceptable health risk. Other reasons for suspension or termination may be made by us based on evolving business objectives and/or the competitive environment.

Information about clinical trials must be submitted within specific timeframes to the NIH for public dissemination on its ClinicalTrials.gov website.

Expanded Access to an Investigational Drug for Treatment Use

Expanded access, sometimes called "compassionate use," is the use of investigational new drug products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. The rules and regulations related to expanded access are intended to improve access to investigational drugs for patients who may benefit from investigational therapies. FDA regulations allow access to investigational drugs under an IND by the company or the treating physician for treatment purposes on a case-by-case basis for: individual patients (single-patient IND applications for treatment in emergency settings and non-emergency settings); intermediate-size patient populations; and larger populations for use of the drug under a treatment protocol or Treatment IND Application.

When considering an IND application for expanded access to an investigational product with the purpose of treating a patient or a group of patients, the sponsor and treating physicians or investigators will determine suitability when all of the following criteria apply: patient(s) have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition; the potential patient benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context or condition to be treated; and the expanded use of the investigational drug for the requested treatment will not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the product or otherwise compromise the potential development of the product.

On December 13, 2016, the 21st Century Cures Act, or the Cures Act, established (and the 2017 Food and Drug Administration Reauthorization Act later amended) a requirement that sponsors of one or more investigational drugs for the treatment of a serious disease(s) or condition(s) make publicly available their policy for evaluating and responding to requests for expanded access for individual patients. Although these requirements were rolled out over time, they have now come into full effect. This provision requires drug and biologic companies to make publicly available their policies for expanded access for individual patient access to products intended for serious diseases. Sponsors are required to make such policies publicly available upon the earlier of initiation of a Phase 2 or Phase 3 study; or 15 days after the drug or biologic receives designation as a breakthrough therapy, fast track product, or regenerative medicine advanced therapy.

In addition, on May 30, 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase I clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act, but the manufacturer must develop an internal policy and respond to patient requests according to that policy.

Human Clinical Trials in Support of an NDA

Clinical trials involve the administration of the investigational product candidate to human subjects under the supervision of a qualified investigator in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written clinical trial protocols detailing, among other things, the objectives of the study, inclusion and exclusion criteria, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

Human clinical trials are typically conducted in three sequential phases, but the phases may overlap or be combined. Additional studies may also be required after approval.

Phase 1 clinical trials are initially conducted in a limited population to test the product candidate for safety, including adverse effects, dose tolerance, absorption, metabolism, distribution, excretion and pharmacodynamics in healthy humans or in patients. During Phase 1 clinical trials, information about the investigational drug product's pharmacokinetics and pharmacological effects may be obtained to permit the design of well-controlled and scientifically valid Phase 2 clinical trials.

Phase 2 clinical trials are generally conducted in a limited patient population to identify possible adverse effects and safety risks, evaluate the efficacy of the product candidate for specific targeted indications and determine dose tolerance and optimal dosage. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more costly Phase 3 clinical trials. Phase 2 clinical trials are well controlled, closely monitored and conducted in a limited patient population.

Phase 3 clinical trials proceed if the Phase 2 clinical trials demonstrate that a dose range of the product candidate is potentially effective and has an acceptable safety profile. Phase 3 clinical trials are undertaken within an expanded patient population to further evaluate dosage, provide substantial evidence of clinical efficacy and further test for safety in an expanded and diverse patient population at multiple, geographically dispersed clinical trial sites. A well-controlled, statistically robust Phase 3 clinical trial may be designed to deliver the data that regulatory authorities will use to decide whether or not to approve, and, if approved, how to appropriately label a drug. Such Phase 3 studies are referred to as "pivotal."

In some cases, the FDA may approve an NDA for a product candidate but require the sponsor to conduct additional clinical trials to further assess the product candidate's safety and effectiveness after approval. Such post-approval trials are typically referred to as Phase 4 clinical trials. These studies are used to gain additional experience from the treatment of a larger number of patients in the intended treatment group and to further document a clinical benefit in the case of drugs approved under accelerated approval regulations. Failure to exhibit due diligence with regard to conducting Phase 4 clinical trials could result in withdrawal of approval for products.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the product; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product has been associated with unexpected serious harm to patients. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

Concurrent with clinical trials, companies often complete additional animal studies. They must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, must develop methods for testing the identity, strength, quality, purity, and potency of the final drug. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

Pediatric Studies

Under the Pediatric Research Equity Act of 2003, an NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. Sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests and other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

For drugs intended to treat a serious or life-threatening disease or condition, the FDA must, upon the request of an applicant, meet to discuss preparation of the initial pediatric study plan or to discuss deferral or waiver of pediatric assessments. In addition, the FDA will meet early in the development process to discuss pediatric study plans with sponsors, and the FDA must meet with sponsors by no later than the end-of-phase 1 meeting for serious or life-threatening diseases and by no later than ninety (90) days after the FDA's receipt of the study plan.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in the Food and Drug Administration Safety and Innovation Act in 2012. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

Review and Approval of an NDA

In order to obtain approval to market a drug product in the United States, a marketing application must be submitted to the FDA that provides sufficient data establishing the safety, purity and potency of the proposed drug product for its intended indication. The application includes all relevant data available from pertinent preclinical and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls and proposed labeling, among other things. Data can come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including studies initiated by independent investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety, purity and potency of the drug product to the satisfaction of the FDA.

The NDA is a vehicle through which applicants formally propose that the FDA approve a new product for marketing and sale in the United States for one or more indications. Every new non-biologic drug product candidate must be the subject of an approved NDA before it may be commercialized in the United States. BLAs are submitted for approval of biologic products. Under federal law, the submission of most NDAs is subject to an application user fee, which for federal fiscal year 2019 is \$2,588,478 for an application requiring clinical data. The sponsor of an approved NDA is also subject to an annual program fee, which for fiscal year 2019 is \$309,915. Certain exceptions and waivers are available for some of these

fees, such as an exception from the application fee for products with orphan designation, an exception from the program fee when the program does not engage in manufacturing the drug during a particular fiscal year and a waiver for certain small businesses.

The FDA conducts a preliminary review of the application, generally within 60 calendar days of its receipt, and strives to inform the sponsor within 74 days whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept the application for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review process of NDAs. Under that agreement, 90% of applications seeking approval of New Molecular Entities, or NMEs, are meant to be reviewed within ten months from the date on which the FDA accepts the application for filing, and 90% of applications for NMEs that have been designated for Priority Review are meant to be reviewed within six months of the filing date. For applications seeking approval of products that are not NMEs, the ten-month and six-month review periods run from the date that the FDA receives the application. The review process and the Prescription Drug User Fee Act, or PDUFA, goal date may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an application, the FDA typically will inspect the facility or facilities where the product is being or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA submission, including component manufacturing, finished product manufacturing and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Under the FDA Reauthorization Act of 2017, the FDA must implement a protocol to expedite review of responses to inspection reports pertaining to certain applications, including applications for products in shortage or those for which approval is dependent on remediation of conditions identified in the inspection report.

In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. A REMS uses risk-minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, the seriousness of the disease, the expected benefit of the product, the expected duration of treatment, the seriousness of known or potential adverse events and whether the product is a new molecular entity.

The FDA may refer an application for a novel product to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that review, evaluate and provide a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but the FDA considers such recommendations carefully when making decisions.

Fast Track, Breakthrough Therapy, Priority Review and Regenerative Advanced Therapy Designations

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are referred to as Fast Track designation, Breakthrough Therapy designation, Priority Review designation and Regenerative Advanced Therapy designation.

Specifically, the FDA may designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition and it demonstrates the potential to address unmet medical needs for such a disease or

condition. For Fast Track products, sponsors may have greater interaction with the FDA, and the FDA may initiate review of sections of a Fast Track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information, and the sponsor must pay applicable user fees. However, the FDA's time-period goal for reviewing a Fast Track application does not begin until the last section of the application is submitted. In addition, the Fast Track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, a product may be designated as a Breakthrough Therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to Breakthrough Therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate a product for Priority Review if it treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A Priority Review designation is intended to direct overall attention and resources to the evaluation of such applications and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

With passage of the Cures Act in December 2016, Congress authorized the FDA to accelerate review and approval of products designated as Regenerative Advanced Therapies. A product is eligible for this designation if it is a regenerative medicine therapy that is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition and if preliminary clinical evidence indicates that the product has the potential to address unmet medical needs for such disease or condition. The benefits of a Regenerative Advanced Therapy designation include early interactions with the FDA to expedite development and review, benefits available to breakthrough therapies, potential eligibility for Priority Review and accelerated approval based on surrogate or intermediate endpoints.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a product for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely, based on epidemiologic, therapeutic, pathophysiologic, or other evidence, to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. Products granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, efficacy biomarker or other measure that is thought to

predict clinical benefit but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a product.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a product, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. The benefit of accelerated approval derives from the potential to receive approval based on surrogate endpoints sooner than possible for trials with clinical or survival endpoints, rather than deriving from any explicit shortening of the FDA approval timeline, as is the case with Priority Review.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the product's clinical benefit. As a result, a product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or to confirm a clinical benefit during post-marketing studies, would allow the FDA to initiate expedited proceedings to withdraw approval of the product. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

The FDA's Decision on an NDA

On the basis of the FDA's evaluation of the application and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If the FDA approves a new product, it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, or require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess the drug's safety after approval. The agency may also require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including a REMS, to help ensure that the benefits of the product outweigh the potential risks. REMS programs can include medication guides, communication plans for health care professionals, and elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring and the use of patent registries. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. The FDA may require a REMS before or after approval if it becomes aware of a serious risk associated with use of the product. The requirement for a REMS can materially affect the potential market and profitability of a product. After approval, many types of changes to the approved product, such as adding new indications, changing manufacturing processes and adding labeling claims, are subject to further testing requirements and FDA review and approval.

Post-Approval Regulation

If regulatory approval for marketing of a product or new indication for an existing product is obtained, the sponsor will be required to comply with all regular post-approval regulatory requirements as well as any post-approval requirements that the FDA may have imposed as part of the approval process. The sponsor will be required to report, among other things, certain adverse reactions and manufacturing problems to the FDA, provide updated safety and efficacy information and comply with requirements concerning advertising and promotional labeling requirements. Manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMP regulations, which impose certain procedural and documentation requirements upon manufacturers. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. Accordingly, the sponsor and its third-party manufacturers must continue to expend time, money and effort in the areas of production and quality control to maintain compliance with cGMP regulations and other regulatory requirements.

A product may also be subject to official lot release, meaning that the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release, the manufacturer must submit to the FDA samples of each lot, together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot. The FDA may also perform certain confirmatory tests on lots of some products before releasing the lots for distribution. Finally, the FDA will conduct laboratory research related to the safety, purity, potency and effectiveness of pharmaceutical products.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates the marketing, labeling, advertising and promotion of prescription drug products placed on the market. This regulation includes, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities, and promotional activities involving the Internet and social media. Promotional claims about a drug's safety or effectiveness are prohibited before the drug is approved. After approval, a drug product generally may not be promoted for uses that are not approved by the FDA, as reflected in the product's prescribing information. In the United States, health care professionals are generally permitted to prescribe drugs for such uses not described in the drug's labeling, known as off-label uses, because the FDA does not regulate the practice of medicine. However, FDA regulations impose rigorous restrictions on manufacturers' communications, prohibiting the promotion of off-label uses. It may be permissible, under very specific, narrow conditions, for a manufacturer to engage in nonpromotional, non-misleading

communication regarding off-label information, such as distributing scientific or medical journal information.

If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the DOJ, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion, and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, and its implementing regulations, as well as the Drug Supply Chain Security Act, or DSCA, which regulate the distribution and tracing of prescription drug samples at the federal level, and set minimum standards for the regulation of distributors by the states. The PDMA, its implementing regulations and state laws limit the distribution of prescription pharmaceutical product samples, and the DSCA imposes requirements to ensure accountability in distribution and to identify and remove counterfeit and other illegitimate products from the market.

Section 505(b)(2) NDAs

NDAs for most new drug products are based on two full clinical studies which must contain substantial evidence of the safety and efficacy of the proposed new product for the proposed use. These applications are submitted under Section 505(b)(1) of the FDCA. The FDA is, however, authorized to approve an alternative type of NDA under Section 505(b)(2) of the FDCA. This type of application allows the applicant to rely, in part, on the FDA's previous findings of safety and efficacy for a similar product, or published literature. Specifically, Section 505(b)(2) applies to NDAs for a drug for which the investigations made to show whether or not the drug is safe for use and effective in use and relied upon by the applicant for approval of the application "were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted."

Thus, Section 505(b)(2) authorizes the FDA to approve an NDA based on safety and effectiveness data that were not developed by the applicant. NDAs filed under Section 505(b)(2) may provide an alternate and potentially more expeditious pathway to FDA approval for new or improved formulations or new uses of previously approved products. If the 505(b)(2) applicant can establish that reliance on the FDA's previous approval is scientifically appropriate, the applicant may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new drug candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress established an abbreviated regulatory scheme authorizing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA pursuant to NDAs. To obtain approval of a generic drug, an applicant must submit an Abbreviated New Drug Application, or ANDA, to the agency. An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the active pharmaceutical ingredient, bioequivalence, drug product formulation, specifications and stability of the generic drug, as well as analytical methods, manufacturing process validation data and quality control procedures. ANDAs are abbreviated because

they generally do not include preclinical and clinical data to demonstrate safety and effectiveness. Instead, in support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference-listed drug, or RLD.

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, route of administration, dosage form, strength and conditions of use of the drug. At the same time, the FDA must also determine that the generic drug is bioequivalent to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if "the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug." Upon approval of an ANDA, the FDA indicates whether the generic product is "therapeutically equivalent" to the RLD in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations," also referred to as the "Orange Book." Physicians and pharmacists consider a therapeutic equivalent generic drug to be fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA's designation of therapeutic equivalence often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or the patient.

Under the Hatch-Waxman Amendments, the FDA may not approve an ANDA until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity. For the purposes of this provision, a new chemical entity, or NCE, is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval.

The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication. Three-year exclusivity would be available for a drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from accepting ANDAs seeking approval for generic versions of the drug as of the date of approval of the original drug product. The FDA typically makes decisions about awards of data exclusivity shortly before a product is approved.

The FDA must establish a Priority Review track for certain generic drugs, requiring the FDA to review a drug application within eight months for a drug that has three or fewer approved drugs listed in the Orange Book and is no longer protected by any patent or regulatory exclusivities, or is on the FDA's drug shortage list. The FDA is also authorized to expedite review of "competitor generic therapies" or drugs with inadequate generic competition, including holding meetings with or providing advice to the drug sponsor prior to submission of the application.

Hatch-Waxman Patent Certification and the 30-Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for

which the ANDA applicant is not seeking approval. To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would.

Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the application will not be approved until all the listed patents claiming the referenced product have expired (other than method of use patents involving indications for which the applicant is not seeking approval).

If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months after the receipt of the Paragraph IV notice, the expiration of the patent, or a decision in the infringement case that is favorable to the ANDA applicant.

To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would. As a result, approval of a Section 505(b)(2) NDA can be stalled until all the listed patents claiming the referenced product have expired, until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired, and, in the case of a Paragraph IV certification and subsequent patent infringement suit, until the earlier of 30 months, settlement of the lawsuit or a decision in the infringement case that is favorable to the Section 505(b)(2) applicant.

Pediatric Exclusivity

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition, generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a product available in the United States for treatment of the disease or condition will be recovered from sales of the product. A company must seek orphan drug designation before submitting an NDA for the candidate product. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan drug designation does not shorten the PDUFA goal dates for the regulatory review and approval process, although it does convey certain advantages such as tax benefits and exemption from the PDUFA application fee.

If a product with orphan designation receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not approve another sponsor's marketing application for the same drug for the same condition for seven years, except in certain limited circumstances. Orphan exclusivity does not block the approval of a different product for the same rare disease or condition, nor does it block the approval of the same product for different conditions. If a drug designated as an orphan drug ultimately receives marketing approval for an indication broader than what was designated in its orphan drug application, it may not be entitled to exclusivity.

Orphan drug exclusivity will not bar approval of another product under certain circumstances, including if a subsequent product with the same drug for the same condition is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand. This is the case despite an earlier court opinion holding that the Orphan Drug Act unambiguously required the FDA to recognize orphan exclusivity regardless of a showing of clinical superiority.

Patent Term Restoration and Extension

A patent claiming a new drug product may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during the FDA regulatory review. The restoration period granted on a patent covering a product is typically one-half the time between the effective date of a clinical investigation involving human beings is begun and the submission date of an application, plus the time between the submission date of an application and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved product is eligible for the extension, and only those claims covering the approved product, a method for using it, or a method for manufacturing it may be extended. Additionally, the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. The United States Patent and Trademark Office reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Health Care Law and Regulation

Health care providers and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, patient privacy laws and regulations and other health care laws and

regulations that may constrain business and/or financial arrangements. Restrictions under applicable federal and state health care laws and regulations, include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal health care program such as Medicare and Medicaid;
- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any health care benefit program or making false statements relating to health care matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal false statements statute, which prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for health care benefits, items or services;
- the Foreign Corrupt Practices Act, or FCPA, which prohibits companies and their intermediaries from making, or offering or promising to make improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment;
- the federal transparency requirements known as the federal Physician Payments Sunshine Act, under the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act, or the ACA, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the United States Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to health care items or services that are reimbursed by non-government third-party payors, including private insurers.

Further, some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. Additionally, some state and local laws require the registration of pharmaceutical sales representatives in the jurisdiction. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Pharmaceutical Insurance Coverage and Health Care Reform

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated health care costs. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage and establish adequate reimbursement levels for, the product. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is approved and have a material adverse effect on sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

The containment of health care costs also has become a priority of federal, state and foreign governments and the prices of products have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and biologics and other medical products, government control and other changes to the health care system in the United States.

In March 2010, the United States Congress enacted the ACA, which, among other things, includes changes to the coverage and payment for drug products under government health care programs. Among the provisions of the ACA of importance to our potential product candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;

- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price" for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices;
- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expanded the types of entities eligible for the 340B drug discount program;
- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 70% point-of-sale-discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least \$1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers up to 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments, will remain in effect through 2027 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Since enactment of the ACA, there have been numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by President Trump on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, is effective as of 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018, among other things, amends the ACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole". The Congress will likely consider other legislation to replace elements of the ACA during the next Congressional session.

In addition, on December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseparable feature of the ACA, and therefore because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. The Trump administration and CMS have both stated that the ruling will have no immediate effect, and on December 30, 2018 the same judge issued an order staying the judgment pending appeal. The Trump Administration has recently represented to the Court of Appeals considering this judgment that it does not oppose the lower court's ruling. It is unclear how this decision and any subsequent appeals and other efforts to repeal and replace the ACA will impact the ACA and our business. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The Trump Administration has also taken executive actions to undermine or delay implementation of the ACA. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. One Executive Order directs federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. The second Executive Order terminates the cost-sharing subsidies that reimburse insurers under the ACA. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. In addition, CMS has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than \$12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. The effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and potentially our business, are not yet known.

Further, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. For example, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs.

For example, on May 11, 2018, the Administration issued a plan to lower drug prices. Under this blueprint for action, the Administration indicated that the Department of Health and Human Services, or HHS, will: take steps to end the gaming of regulatory and patent processes by drug makers to unfairly protect monopolies; advance biosimilars and generics to boost price competition; evaluate the inclusion of prices in drug makers' advertisements to enhance price competition; speed access to and lower the cost of new drugs by clarifying policies for sharing information between insurers and drug makers; avoid excessive pricing by relying more on value-based pricing by expanding outcome-based payments in Medicare and Medicaid; work to give Part D plan sponsors more negotiation power with drug makers; examine which Medicare Part B drugs could be negotiated for a lower price by Part D plans, and improving the design of the Part B Competitive Acquisition Program; update Medicare's drug-pricing dashboard to increase transparency; prohibit Part D contracts that include "gag rules" that prevent pharmacists from informing patients when they could pay less out-of-pocket by not using insurance; and require that Part D plan

members be provided with an annual statement of plan payments, out-of-pocket spending, and drug price increases. More recently, on January 31, 2019, the HHS Office of Inspector General proposed modifications to the federal Anti-Kickback Statute discount safe harbor for the purpose of reducing the cost of drug products to consumers which, among other things, if finalized, will affect discounts paid by manufacturers to Medicare Part D plans, Medicaid managed care organizations and pharmacy benefit managers working with these organizations.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Review and Approval of Medicinal Products in the European Union

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of products. Whether or not it obtains FDA approval for a product, an applicant will need to obtain the necessary approvals by the comparable non-U.S. regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. The approval process ultimately varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others. Specifically, however, the process governing approval of medicinal products in the European Union, or EU, generally follows the same lines as in the United States. It entails satisfactory completion of preclinical studies and adequate and well-controlled clinical trials to establish the safety and efficacy of the product for each proposed indication. It also requires the submission to the relevant competent authorities of an MAA and granting of a marketing authorization by these authorities before the product can be marketed and sold in the EU.

Clinical Trial Approval

The Clinical Trials Directive 2001/20/EC, the Directive 2005/28/EC on GCP and the related national implementing provisions of the individual member states of the European Union, or EU Member States, govern the system for the approval of clinical trials in the EU. Under this system, an applicant must obtain prior approval from the competent national authority of the EU Member States in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion. The clinical trial application must be accompanied by, among other documents, an investigational medicinal product dossier (the Common Technical Document) with supporting information prescribed by Directive 2001/20/EC, Directive 2005/28/EC, where relevant the implementing national provisions of the individual EU Member States and further detailed in applicable guidance documents.

In April 2014, the new Clinical Trials Regulation, (EU) No 536/2014, was adopted. The Clinical Trials Regulation was published on June 16, 2014 but is not expected to apply until later in 2019. The Clinical Trials Regulation will be directly applicable in all the EU Member States, repealing the current Clinical Trials Directive 2001/20/EC and replacing any national legislation that was put in place to implement the Directive. Conduct of all clinical trials performed in the EU will continue to be bound by currently applicable provisions until the new Clinical Trials Regulation becomes applicable. The extent to which on-going clinical trials will be governed by the Clinical Trials Regulation will depend on when the Clinical Trials Regulation becomes applicable and on the duration of the individual clinical trial. If a clinical trial continues for more than three years from the day on which the Clinical Trials Regulation becomes applicable the Clinical Trials Regulation will at that time begin to apply to the clinical trial.

The new Clinical Trials Regulation aims to simplify and streamline the approval of clinical trials in the EU. The main characteristics of the regulation include: a streamlined application procedure via a single entry point, the "EU Portal and Database"; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed by the appointed reporting Member State, whose assessment report is submitted for review by the sponsor and all other competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted (Concerned Member States). Part II is assessed separately by each Concerned Member State. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the Concerned Member State. However, overall related timelines will be defined by the Clinical Trials Regulation.

PRIME Designation in the EU

In March 2016, the EMA launched an initiative to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRiority Medicines, or PRIME, scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises, or SMEs, may qualify for earlier entry into the PRIME scheme than larger companies. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated MAA assessment once a dossier has been submitted. Importantly, a dedicated Agency contact and rapporteur from the Committee for Human Medicinal Products, or CHMP, or Committee for Advanced Therapies, are appointed early in PRIME scheme facilitating increased understanding of the product at EMA's Committee level. A kick-off meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

Marketing Authorization

To obtain a marketing authorization for a product under EU regulatory systems, an applicant must submit an MAA either under a centralized procedure administered by the EMA, or one of the procedures administered by competent authorities in the EU Member States (decentralized procedure, national procedure or mutual recognition procedure). A marketing authorization may be granted only to an applicant established in the EU. Regulation (EC) No 1901/2006 provides that prior to obtaining a marketing authorization in the EU, applicants have to demonstrate compliance with all measures included in an EMA-approved Paediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted (1) a product-specific waiver, (2) a class waiver or (3) a deferral for one or more of the measures included in the PIP.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid across the European Economic Area (i.e. the EU as well as Iceland, Liechtenstein and Norway). Pursuant to Regulation (EC) No 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy medicinal products and products with a new active substance indicated for the treatment of certain diseases. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional. The centralized procedure may at the request of the applicant also be used in certain other cases. We anticipate that the centralized procedure will be mandatory for the product candidates we are developing.

Under the centralized procedure, the CHMP is responsible for conducting the initial assessment of a product and for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the EU, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. If the CHMP accepts such request, the time limit of 210 days will be reduced to 150 days but it is possible that the CHMP can revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment. At the end of this period, the CHMP provides a scientific opinion on whether or not a marketing authorization should be granted in relation to a medicinal product. Within 15 calendar days of receipt of a final opinion from the CHMP, the European Commission must prepare a draft decision concerning an application for marketing authorization. This draft decision must take the opinion and any relevant provisions of EU law into account. Before arriving at a final decision on an application for centralized authorization of a medicinal product the European Commission must consult the Standing Committee on Medicinal Products for Human Use. The Standing Committee is composed of representatives of the EU Member States and chaired by a non-voting European Commission representative. The European Parliament also has a related "droit de regard". The European Parliament's role is to ensure that the European Commission has not exceeded its powers in deciding to grant or refuse to grant a marketing authorization.

The European Commission may grant a so-called "marketing authorization under exceptional circumstances". Such authorization is intended for products for which the applicant can demonstrate that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use, because the indications for which the product in question is intended are encountered so rarely that the applicant cannot reasonably be expected to provide comprehensive evidence, or in the present state of scientific knowledge, comprehensive information cannot be provided, or it would be contrary to generally accepted principles of medical ethics to collect such information. Consequently, marketing authorization under exceptional circumstances may be granted subject to certain specific obligations, which may include the following:

- the applicant must complete an identified program of studies within a time period specified by the competent authority, the results of which form the basis of a reassessment of the benefit/risk profile;
- the medicinal product in question may be supplied on medical prescription only and may in certain cases be administered only under strict medical supervision, possibly in a hospital and in the case of a radiopharmaceutical, by an authorized person; and
- the package leaflet and any medical information must draw the attention of the medical practitioner to the fact that the particulars available concerning the medicinal product in question are as yet inadequate in certain specified respects.

A marketing authorization under exceptional circumstances is subject to annual review to reassess the risk-benefit balance in an annual reassessment procedure. Continuation of the authorization is linked to the annual reassessment and a negative assessment could potentially result in the marketing authorization being suspended or revoked. The renewal of a marketing authorization of a medicinal product under exceptional circumstances, however, follows the same rules as a "normal" marketing authorization. Thus, a marketing authorization under exceptional circumstances is granted for an initial five years, after which the authorization will become valid indefinitely, unless the EMA decides that safety grounds merit one additional five-year renewal.

The European Commission may also grant a so-called "conditional marketing authorization" prior to obtaining the comprehensive clinical data required for an application for a full marketing authorization. Such conditional marketing authorizations may be granted for product candidates (including medicines designated as orphan medicinal products), if (i) the risk-benefit balance of the product candidate is positive, (ii) it is likely that the applicant will be in a position to provide the required comprehensive clinical trial data, (iii) the product fulfills an unmet medical need and (iv) the benefit to public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required. A conditional marketing authorization may contain specific obligations to be fulfilled by the marketing authorization holder, including obligations with respect to the completion of ongoing or new studies, and with respect to the collection of pharmacovigilance data. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions and/or specific obligations. The timelines for the centralized procedure described above also apply with respect to the review by the CHMP of applications for a conditional marketing authorization.

The EU medicines rules expressly permit the EU Member States to adopt national legislation prohibiting or restricting the sale, supply or use of any medicinal product containing, consisting of or derived from a specific type of human or animal cell, such as embryonic stem cells. While the products we have in development do not make use of embryonic stem cells, it is possible that the national laws in certain EU Member States may prohibit or restrict us from commercializing our products, even if they have been granted an EU marketing authorization.

Unlike the centralized authorization procedure, the decentralized marketing authorization procedure requires a separate application to, and leads to separate approval by, the competent authorities of each EU Member State in which the product is to be marketed. This application is identical to the application that would be submitted to the EMA for authorization through the centralized procedure. The reference EU Member State prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. The resulting assessment report is submitted to the concerned EU Member States who, within 90 days of receipt, must decide whether to approve the assessment report and related materials. If a concerned EU Member State cannot approve the assessment report and related materials due to concerns relating to a potential serious risk to public health, disputed elements may be referred to the European Commission, whose decision is binding on all EU Member States.

The mutual recognition procedure similarly is based on the acceptance by the competent authorities of the EU Member States of the marketing authorization of a medicinal product by the competent authorities of other EU Member States. The holder of a national marketing authorization may submit an application to the competent authority of an EU Member State requesting that this authority recognize the marketing authorization delivered by the competent authority of another EU Member State.

Regulatory Data Protection in the EU

In the EU, innovative medicinal products approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity pursuant to Directive 2001/83/EC. Regulation (EC) No 726/2004 repeats

this entitlement for medicinal products authorized in accordance the centralized authorization procedure. Data exclusivity prevents applicants for authorization of generics of these innovative products from referencing the innovator's data to assess a generic (abridged) application for a period of eight years. During an additional two-year period of market exclusivity, a generic MAA can be submitted and authorized, and the innovator's data may be referenced, but no generic medicinal product can be placed on the EU market until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be an NCE so that the innovator gains the prescribed period of data exclusivity, another company nevertheless could also market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Periods of Authorization and Renewals

A marketing authorization has an initial validity for five years in principle. The marketing authorization may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the EU Member State. To this end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. The European Commission or the competent authorities of the EU Member States may decide, on justified grounds relating to pharmacovigilance, to proceed with one further five-year period of marketing authorization. Once subsequently definitively renewed, the marketing authorization shall be valid for an unlimited period. Any authorization which is not followed by the actual placing of the medicinal product on the EU market (in case of centralized procedure) or on the market of the authorizing EU Member State within three years after authorization ceases to be valid (the so-called sunset clause).

Paediatric Studies and Exclusivity

Prior to obtaining a marketing authorization in the European Union, applicants must demonstrate compliance with all measures included in an EMA-approved PIP covering all subsets of the paediatric population, unless the EMA has granted a product-specific waiver, a class waiver, or a deferral for one or more of the measures included in the PIP. The respective requirements for all marketing authorization procedures are laid down in Regulation (EC) No 1901/2006, the so-called Paediatric Regulation. This requirement also applies when a company wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorized. The Paediatric Committee of the EMA, or PDCO, may grant deferrals for some medicines, allowing a company to delay development of the medicine for children until there is enough information to demonstrate its effectiveness and safety in adults. The PDCO may also grant waivers when development of a medicine for children is not needed or is not appropriate, such as for diseases that only affect the elderly population. Before an MAA can be filed, or an existing marketing authorization can be amended, the EMA determines that companies actually comply with the agreed studies and measures listed in each relevant PIP. If an applicant obtains a marketing authorization in all EU Member States, or a marketing authorization granted in the centralized procedure by the European Commission, and the study results for the paediatric population are included in the product information, even when negative, the medicine is then eligible for an additional six-month period of qualifying patent protection through extension of the term of the Supplementary Protection Certificate.

Orphan Drug Designation and Exclusivity

Regulation (EC) No. 141/2000, as implemented by Regulation (EC) No. 847/2000 provides that a drug can be designated as an orphan drug by the European Commission if its sponsor can establish: that the product is intended for the diagnosis, prevention or treatment of (1) a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the EU when the application is made, or (2) a life-threatening, seriously debilitating or serious and chronic condition in the EU and that without incentives it is unlikely that the marketing of the drug in the EU would generate sufficient return to justify the necessary investment. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the EU or, if such method exists, the drug will be of significant benefit to those affected by that condition.

Once authorized, orphan medicinal products are entitled to ten years of market exclusivity in all EU Member States and in addition a range of other benefits during the development and regulatory review process including scientific assistance for study protocols, authorization through the centralized marketing authorization procedure covering all member countries and a reduction or elimination of registration and marketing authorization fees. However, marketing authorization may be granted to a similar medicinal product with the same orphan indication during the ten-year period with the consent of the marketing authorization holder for the original orphan medicinal product or if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities. Marketing authorization may also be granted to a similar medicinal product with the same orphan indication if this product is safer, more effective or otherwise clinically superior to the original orphan medicinal product. The period of market exclusivity may, in addition, be reduced to six years if it can be demonstrated on the basis of available evidence that the original orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity.

Regulatory Requirements After a Marketing Authorization has been Obtained

In case an authorization for a medicinal product in the EU is obtained, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include:

- Compliance with the EU's stringent pharmacovigilance or safety reporting rules must be ensured. These rules can impose post-authorization studies and additional monitoring obligations.
- The manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the applicable EU laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice. These requirements include compliance with EU cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the EU with the intention to import the active pharmaceutical ingredients into the EU.
- The marketing and promotion of authorized drugs, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the EU notably under Directive 2001/83EC, as amended, and are also subject to EU Member State laws. Direct-to-consumer advertising of prescription medicines is prohibited across the EU.

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the EU, commonly referred to as Brexit. Thereafter, on March 29, 2017, the country formally notified the EU of its intention

to withdraw pursuant to Article 50 of the Lisbon Treaty. The withdrawal of the United Kingdom from the EU was meant to take effect either on the effective date of the withdrawal agreement or, in the absence of agreement, two years after the United Kingdom provides a notice of withdrawal pursuant to the EU Treaty, which was March 29, 2019. That date has now been extended to October 31, 2019. Discussions between the United Kingdom and the European Union have focused on finalizing withdrawal issues and transition agreements, but have been extremely difficult to date. Limited progress to date in these negotiations and ongoing uncertainty within the UK Government and Parliament sustains the possibility of the United Kingdom leaving the European Union on the given deadline without a withdrawal agreement and associated transition period in place, which is likely to cause significant market and economic disruption.

Since the regulatory framework for pharmaceutical products in the United Kingdom covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from EU directives and regulations, Brexit could materially impact the future regulatory regime that applies to products and the approval of product candidates in the United Kingdom. It remains to be seen how, if at all, Brexit will impact regulatory requirements for product candidates and products in the United Kingdom.

General Data Protection Regulation

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the EU General Data Protection Regulation, or GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the U.S., and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR will be a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance.

Pricing Decisions for Approved Products

In the EU, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, EU Member States have the option to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. EU Member States may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other EU Member States allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the EU have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage health care expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the EU. The downward pressure on health care costs in general, particularly prescription products, has become intense.

As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU Member States, and parallel trade, i.e., arbitrage between low-priced and high-priced EU Member States, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries.

Employees

As of June 15, 2019, we had 62 full-time employees, including a total of 28 employees with M.D. or Ph.D. degrees. Of these full-time employees, 47 employees are engaged in research and development. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Facilities

Our principal facilities consist of office and laboratory space. We occupy approximately 28,731 square feet of office space in Cambridge, Massachusetts under a lease that currently expires in June 2028.

Legal Proceedings

We are not currently subject to any material legal proceedings.

MANAGEMENT

Executive Officers and Directors

The following table sets forth the name, age as of June 15, 2019 and position of each of our executive officers and directors.

Name	Age	Position
Robert J. Gould, Ph.D.	64	Chief Executive Officer and President, Director
Bryan Stuart	42	Chief Operating Officer
Owen Wallace, Ph.D.	50	Chief Scientific Officer
Diego Cadavid, M.D.	53	Senior Vice President, Clinical Development
Mark Levin ⁽²⁾⁽³⁾	68	Chairman of the Board of Directors
James J. Collins, Ph.D. ⁽³⁾	53	Director
Alan Ezekowitz, MBChB, D.Phil ⁽¹⁾⁽²⁾	65	Director
James Geraghty ⁽¹⁾⁽²⁾⁽³⁾	64	Director
Kate Haviland ⁽¹⁾	43	Director

- (1) Member of the Audit Committee.
- (2) Member of the Compensation Committee.
- (3) Member of the Nominating and Corporate Governance Committee.

Executive Officers

Robert J. Gould, Ph.D. has served as our president and chief executive officer and as a member of our board of directors since June 2016. Dr. Gould previously served as president and chief executive officer of Epizyme, Inc., or Epizyme, a biopharmaceutical company, from March 2010 to September 2015. Prior to joining Epizyme, he served as director of novel therapeutics at the Broad Institute of Massachusetts Institute of Technology, or MIT, and Harvard, a research institute, from December 2006 to March 2010. Dr. Gould spent 23 years at Merck Research Laboratories, or Merck, a healthcare company, where he held a variety of leadership positions, culminating in the role of vice president, licensing and external research. Dr. Gould received a B.A. from Spring Arbor University and a Ph.D. from the University of Iowa and completed postdoctoral studies at the Johns Hopkins University. We believe that Dr. Gould's extensive leadership experience in the life sciences industry and his extensive knowledge of our company based on his current role as our chief executive officer qualify him to serve on our board of directors.

Bryan Stuart has served as our chief operating officer since December 2018. Mr. Stuart previously served as president and chief executive officer of Yarra Therapeutics, LLC, or Yarra, a subsidiary of Array Biopharma, Inc., a biopharmaceutical company focused on genetically defined rare diseases, from December 2017 to August 2018. Prior to joining Yarra, Mr. Stuart served as president of Kastle Therapeutics, LLC, or Kastle, a biopharmaceutical company focused on developing and commercializing treatments for rare diseases, from July 2015 to March 2017 and as president and chief executive officer from March 2017 to November 2017. Prior to joining Kastle, Mr. Stuart was the chief business officer of Civitas Therapeutics, Inc., a biopharmaceutical company, from August 2012 to October 2014, where he led the business development, capital raising, commercial and portfolio management functions, including the sale of Civitas to Acorda Therapeutics, Inc. He previously led business development, corporate development and strategy at both EKR Therapeutics Inc. (acquired by Chiesi Farmaceutici S.p.A.) and Ovation Pharmaceuticals Inc. (acquired by Lundbeck A/S), where he played key roles in each company's growth and ultimate sale. Mr. Stuart began his career as a healthcare investment banker at William Blair & Company. Mr. Stuart received an MBA from the Kellogg School of Management at Northwestern University and a B.S. from the University of Illinois.

Owen Wallace, Ph.D. has served as our chief scientific officer since April 2017. Dr. Wallace previously served as head, global discovery chemistry at Novartis Institutes for BioMedical Research, or Novartis Institutes, a pharmaceutical company, from May 2013 to April 2017. Prior to joining Novartis Institutes, he

held various positions at Eli Lilly & Company, a pharmaceutical company, including site scientific leader and group senior director from July 2010 to June 2013, senior director, discovery chemistry from August 2009 to July 2010, director, discovery chemistry from December 2005 to August 2009 and head, discovery chemistry research from February 2002 to December 2005. Prior to that, Dr. Wallace was a senior research investigator at Bristol-Myers Squibb, a biopharmaceutical company, from March 1995 to May 2000. Dr. Wallace received his Ph.D. in Organic Chemistry from Yale University and his B.Sc. (Hons) in Chemistry from University College Cork in Ireland.

Diego Cadavid, M.D. has served as our senior vice president, clinical development since July 2018 and served as our vice president, clinical development from September 2016 to July 2018. Dr. Cadavid currently serves as an adjunct professor at the University of Massachusetts Medical School. Dr. Cadavid previously served as senior medical director in the MS Clinical Development Group at Biogen Inc., or Biogen, a biotechnology company, from January 2014 to September 2016 and as a director of the Neurology Clinical Group at Biogen from April 2008 to December 2013. Before joining Biogen, Dr. Cadavid spent nine years at Rutgers-New Jersey Medical School where he was Associate Professor of Neurology and Neuroscience. While working at Biogen, Dr. Cadavid served as a consultant at the Center for Immunology and Inflammatory Diseases at the Massachusetts General Hospital in Boston. Dr. Cadavid received an M.D. from Pontificia Universidad Javeriana in Bogota, Colombia.

Non-Employee Directors

Mark Levin has served as a member of our board of directors since August 2015 and chairman of our board of directors since August 2016. Mr. Levin currently serves as a partner at Third Rock Ventures, LLC, which he co-founded in 2007. Mr. Levin served as our interim president and chief executive officer from August 2015 to July 2016 and as interim president and chief executive officer of Voyager Therapeutics, Inc., or Voyager, a biotechnology company, from June 2013 to September 2014. He has served as the chairman of the board of directors of Voyager since June 2013. Mr. Levin was formerly on the boards of publicly traded life sciences companies Eleven Biotherapeutics, Inc. from September 2008 to November 2014 and Foundation Medicine, Inc. from 2010 to June 2014. Mr. Levin served as founding chief executive officer of Millennium Pharmaceuticals, Inc., a biopharmaceutical company since acquired by Takeda Pharmaceutical Company Limited, from 1993 to 2005. Mr. Levin received both a B.S. and an M.S. in Chemical and Biochemical Engineering from Washington University in St. Louis. We believe Mr. Levin's experience working with and serving on the boards of directors of life sciences companies and his experience working in the venture capital industry qualifies him to serve on our board of directors.

James J. Collins, Ph.D. has served on our board of directors since January 2017. Dr. Collins has served as the Termeer Professor of Medical Engineering and Science in the Institute for Medical Engineering and Science and the Department of Biological Engineering at MIT since December 2014. Prior to his joining MIT, from October 1990 to November 2014, Dr. Collins served as a professor in biomedical engineering at Boston University. Dr. Collins received a B.S. in Physics from the College of the Holy Cross and a doctorate in Medical Engineering from the University of Oxford. From 1987 to 1990, he was a Rhodes Scholar. We believe Dr. Collins' extensive industry expertise qualifies him to serve on our board of directors.

Alan Ezekowitz, MBChB, D.Phil has served on our board of directors since December 2016. Dr. Ezekowitz served as the president and chief executive officer of Abide Therapeutics, Inc., or Abide, a biopharmaceutical company that he co-founded, from 2011 to May 2019, when Abide was acquired by H. Lundbeck A/S. Prior to founding Abide, Dr. Ezekowitz was the senior vice president and franchise head for disease areas including bone, respiratory, immunology, muscle, dermatology and urology at Merck from March 2006 to March 2011. Prior to joining Merck, Dr. Ezekowitz was the Charles Wilder Professor of Pediatrics at the Harvard Medical School from June 1995 to March 2005 and served as the chief of pediatric services at the Massachusetts General Hospital for Children and the Partners Healthcare System. Additionally, he directed the Laboratory of Developmental Immunology at Massachusetts General Hospital. Dr. Ezekowitz received his medical training at the University of Cape Town in South Africa and

received a Doctor of Philosophy degree from Oxford University. We believe Dr. Ezekowitz's leadership experience in the life sciences industry qualifies him to serve on our board of directors.

James Geraghty has served on our board of directors since July 2016. Mr. Geraghty is an industry leader with over 30 years of strategic and leadership experience, including more than 20 years as a senior member of executive teams at biotechnology companies developing and commercializing innovative therapies. From May 2013 to December 2016, Mr. Geraghty was an Entrepreneur in Residence at Third Rock Ventures, a leading biotech venture and company-formation fund. From April 2011 to December 2012, Mr. Geraghty served as a senior vice president of Sanofi, a global healthcare company. Prior to that, he served in various senior management roles at Genzyme Corporation, or Genzyme, a biotechnology company, from 1992 to April 2011, including as senior vice president, international development from January 2007 to April 2011. Mr. Geraghty currently serves as chairman of the board of directors of Orchard Therapeutics plc, Idera Pharmaceuticals, Inc., or Idera, and Pieris Pharmaceuticals, Inc., each publicly traded companies, and as a member of the board of directors of Voyager, a publicly traded company. He previously served as chairman of the board of Juniper Pharmaceuticals, Inc. and as a director of bluebird bio Inc. and GTC Biotherapeutics, Inc. Mr. Geraghty received a B.A. in English from Georgetown University, an M.S. in Psychology from the University of Pennsylvania and a J.D. From Yale Law School. We believe Mr. Geraghty's public company board and management experience and his broad and deep knowledge of the industry in which we operate qualifies him to serve on our board of directors.

Kate Haviland has served on our board of directors since June 2018. Ms. Haviland has served as chief operating officer of Blueprint Medicines Corporation, or Blueprint, a precision therapy company, since February 2019. Prior to her serving as chief operating officer, Ms. Haviland served as chief business officer of Blueprint from January 2016 to January 2019. Prior to that, from April 2014 to December 2015, Ms. Haviland served as vice president, rare diseases and oncology program leadership at Idera, a clinical-stage biopharmaceutical company, where she oversaw all aspects of the product development strategy for Idera's rare disease and oncology pipeline programs, including preclinical research, manufacturing and drug supply, regulatory affairs, clinical development and execution and commercial planning. Prior to joining Idera, from June 2012 to April 2014, Ms. Haviland served as head of commercial development at Sarepta Therapeutics, Inc., a commercial-stage biopharmaceutical company, where she was responsible for product development and commercial planning and for cultivating relationships with key opinion leaders and patient advocacy groups. In addition, Ms. Haviland previously served as executive director of commercial development at PTC Therapeutics, Inc., a biopharmaceutical company, from March 2007 to June 2012 and held corporate development and project management roles at Genzyme, a biotechnology company, from July 2005 to April 2007. Ms. Haviland received a B.A. from Wesleyan University with a double major in biochemistry/molecular biology and economics and an M.B.A. from Harvard Business School. We believe Ms. Haviland's extensive experience working with life sciences companies qualifies her to serve on our board of directors.

Board Composition and Election of Directors

Board Composition

Our board of directors is currently authorized to have eight members and currently consists of six members. Upon the closing of this offering, we will reduce the authorized number of members of our board of directors to six. Our directors hold office until their successors have been elected and qualified or until the earlier of their death, resignation or removal.

Our certificate of incorporation and bylaws that will become effective upon the closing of this offering provide that the authorized number of directors may be changed only by resolution of our board of directors. Our certificate of incorporation and bylaws will also provide that our directors may be removed only for cause by the affirmative vote of the holders of 75% of our shares of capital stock present in person or by proxy and entitled to vote, and that any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office.

In accordance with the terms of our certificate of incorporation and bylaws that will become effective upon the closing of this offering, our board of directors will be divided into three classes, class I, class II and class III, with members of each class serving staggered three-year terms. Upon the closing of this offering, the members of the classes will be divided as follows:

- the class I directors will be Alan Ezekowitz and Mark Levin, and their term will expire at the annual meeting of stockholders to be held in 2020;
- the class II directors will be James Collins and James Geraghty, and their term will expire at the annual meeting of stockholders to be held in 2021; and
- the class III directors will be Robert Gould and Kate Haviland, and their term will expire at the annual meeting of stockholders to be held in 2022.

Upon the expiration of the term of a class of directors, directors in that class will be eligible to be elected for a new three-year term at the annual meeting of stockholders in the year in which their term expires.

The classification of our board of directors may have the effect of delaying or preventing changes in our control or management. See "Description of Capital Stock—Delaware Anti-Takeover Law and Certain Charter and Bylaw Provisions."

Director Independence

Applicable Nasdaq rules require a majority of a listed company's board of directors to be comprised of independent directors within one year of listing. In addition, Nasdaq rules require that, subject to specified exceptions, each member of a listed company's audit, compensation and nominating and corporate governance committees be independent under the Securities Exchange Act of 1934, as amended, or the Exchange Act. Audit committee members must also satisfy the independence criteria set forth in Rule 10A-3 under the Exchange Act and compensation committee members must also satisfy the independence criteria set forth in Rule 10C-1 under the Exchange Act. Under applicable Nasdaq rules, a director will only qualify as an "independent director" if, in the opinion of the listed company's board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In order to be considered independent for purposes of Rule 10A-3, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board committee, accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries or otherwise be an affiliated person of the listed company or any of its subsidiaries. In order to be considered independent for purposes of Rule 10C-1, the board must consider, for each member of a compensation committee of a listed company, all factors specifically relevant to determining whether a director has a relationship to such company which is material to that director's ability to be independent from management in connection with the duties of a compensation committee member, including, but not limited to: (1) the source of compensation of the director, including any consulting advisory or other compensatory fee paid by such company to the director; and (2) whether the director is affiliated with the company or any of its subsidiaries or affiliates.

In June 2019, our board of directors undertook a review of the composition of our board of directors and its committees and the independence of each director. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our board of directors has determined that each of our directors, with the exception of Dr. Gould, is an "independent director" as defined under applicable Nasdaq rules, including, in the case of all the members of our audit committee, the independence criteria set forth in Rule 10A-3 under the Exchange Act, and in the case of all the members of our compensation committee, the independence criteria set forth in Rule 10C-1 under the Exchange Act. In making such determination, our board of directors considered the relationships that each such non-employee director has with our company and all other facts and circumstances that our board of directors deemed relevant in determining his or her

independence, including the beneficial ownership of our capital stock by each non-employee director. Dr. Gould is not an independent director under these rules because he is our president and chief executive officer.

There are no family relationships among any of our directors or executive officers.

Board Committees

Our board of directors has established an audit committee, a compensation committee and a nominating and corporate governance committee, each of which operates under a charter that has been approved by our board. The composition of each committee will be effective as of the date of this prospectus.

Audit Committee

The members of our audit committee are Alan Ezekowitz, James Geraghty and Kate Haviland. Alan Ezekowitz is the chair of the audit committee. Effective at the time of this offering, our audit committee's responsibilities will include:

- appointing, approving the compensation of, and assessing the independence of our registered public accounting firm;
- overseeing the work of our independent registered public accounting firm, including through the receipt and consideration of reports from that firm;
- reviewing and discussing with management and our independent registered public accounting firm our annual and quarterly financial statements and related disclosures;
- monitoring our internal control over financial reporting, disclosure controls and procedures and code of business conduct and ethics;
- overseeing our risk assessment and risk management policies;
- establishing procedures for the receipt and retention of accounting related complaints and concerns;
- meeting independently with our internal auditing staff, if any, our independent registered public accounting firm and management;
- reviewing and approving or ratifying any related person transactions; and
- preparing the audit committee report required by SEC rules.

All audit and non-audit services, other than *de minimis* non-audit services, to be provided to us by our independent registered public accounting firm must be approved in advance by our audit committee.

Our board of directors has determined that we do not have an "audit committee financial expert" as defined by applicable SEC rules serving on our audit committee. Our board of directors believes that, given the size and stage of development of our company, an audit committee financial expert is not necessary at this time because the collective financial and business expertise of the members of the audit committee is sufficient to satisfy the functions of the audit committee under the terms of the audit committee charter. In making this determination, our board of directors considered the formal education and nature and scope of our audit committee members' previous experience. We believe that the composition of our audit committee will meet the requirements for independence under current Nasdaq and SEC rules and regulations.

Compensation Committee

The members of our compensation committee are Mark Levin, Alan Ezekowitz and James Geraghty. Mark Levin is the chair of the compensation committee. Effective at the time of this offering, our compensation committee's responsibilities will include:

- reviewing and approving, or making recommendations to our board of directors with respect to, the compensation of our chief executive officer and our other executive officers;
- overseeing an evaluation of our senior executives;
- overseeing and administering our cash and equity incentive plans;
- reviewing and making recommendations to our board of directors with respect to director compensation;
- reviewing and discussing annually with management our "Compensation Discussion and Analysis" disclosure if and to the extent then required by SEC rules; and
- preparing the compensation committee report if and to the extent then required by SEC rules.

We believe that the composition of our compensation committee will meet the requirements for independence under current Nasdaq and SEC rules and regulations.

Nominating and Corporate Governance Committee

The members of our nominating and corporate governance committee are James Geraghty, James Collins and Mark Levin. James Geraghty is the chair of the nominating and corporate governance committee. Effective at the time of this offering, our nominating and corporate governance committee's responsibilities will include:

- recommending to our board of directors the persons to be nominated for election as directors and to each of our board's committees;
- reviewing and making recommendations to our board with respect to our board leadership structure;
- reviewing and making recommendations to our board with respect to management succession planning;
- developing and recommending to our board of directors corporate governance principles; and
- overseeing an annual evaluation of our board of directors.

We believe that the composition of our nominating and corporate governance committee will meet the requirements for independence under current Nasdaq and SEC rules and regulations.

Compensation Committee Interlocks and Insider Participation

None of our executive officers serves, or in the past year has served, as a member of the board of directors or compensation committee, or other committee serving an equivalent function, of any other entity that has one or more of its executive officers serving as a member of our board of directors or our compensation committee. None of the members of our compensation committee is, or has ever been, an officer or employee of our company.

Code of Ethics and Code of Conduct

We have adopted a written code of business conduct and ethics, which will be effective at the time of this offering, that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. We intend to post a current copy of the code on our website, www.fulcrumtx.com. In addition, we intend to post on our website all disclosures that are required by law or Nasdaq listing standards concerning any amendments to, or waivers from, any provision of the code.

EXECUTIVE COMPENSATION

The following discussion relates to the compensation of our president and chief executive officer, Robert J. Gould, our chief operating officer, Bryan Stuart, and our senior vice president, clinical development, Diego Cadavid, for fiscal year 2018. Dr. Gould, Mr. Stuart and Dr. Cadavid are collectively referred to in this prospectus as our named executive officers.

In preparing to become a public company, we have begun a thorough review of all elements of our executive compensation program, including the function and design of our equity incentive programs. We have begun, and expect to continue in the coming months, to evaluate the need for revisions to our executive compensation program to ensure that our program is competitive with the companies with which we compete for executive talent and is appropriate for a public company.

Summary Compensation Table

The following table sets forth information regarding compensation awarded to, earned by or paid to each of our named executive officers for the year ended December 31, 2018.

<u>Name and Principal Position</u>	<u>Year</u>	<u>Salary (\$)</u>	<u>Bonus \$(¹)</u>	<u>Stock awards \$(²)</u>	<u>Option awards \$(³)</u>	<u>Total (\$)</u>
Robert J. Gould <i>President and Chief Executive Officer</i>	2018	442,900	203,734	207,000	—	853,634
Bryan Stuart ⁽⁴⁾ <i>Chief Operating Officer</i>	2018	16,667	—	—	1,685,290	1,701,957
Diego Cadavid <i>Senior Vice President, Clinical Development</i>	2018	348,383	111,825	27,600	62,556	550,364

- (1) Except where noted otherwise, the amounts reported in the "Bonus" column reflect discretionary annual cash bonuses paid to our named executive officers for their performance.
- (2) The amounts reported in the "Stock awards" column reflect the aggregate fair value of stock-based compensation awarded during the year computed in accordance with the provisions of Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 718. See Note 8 to our consolidated financial statements appearing at the end of this prospectus regarding assumptions underlying the valuation of equity awards.
- (3) The amounts reported in the "Option awards" column reflect the aggregate fair value of stock-based compensation awarded during the year computed in accordance with the provisions of FASB ASC Topic 718. See Note 8 to our consolidated financial statements appearing at the end of this prospectus regarding assumptions underlying the valuation of equity awards. These amounts reflect the accounting cost for these stock options and do not reflect the actual economic value that may be realized by the named executive officer upon the vesting of the stock options, the exercise of the stock options or the sale of the common stock underlying such stock options.
- (4) Mr. Stuart commenced employment with us on December 17, 2018.

Narrative to Summary Compensation Table

Base Salary. In 2018, we paid Dr. Gould an annualized base salary of \$442,900. In January 2019, our board of directors set Dr. Gould's 2019 annual base salary at \$460,000. In 2018, we paid Mr. Stuart an annualized base salary of \$400,000. In January 2019, our board of directors set Mr. Stuart's 2019 annual base salary at \$400,000. In 2018, we paid Dr. Cadavid an annualized base salary of \$342,784 until July 16, 2018, after which Dr. Cadavid was promoted to the position of senior vice president, clinical development,

and we paid Dr. Cadavid an annualized base salary of \$355,000. In January 2019, our board of directors set Dr. Cadavid's 2019 annual base salary at \$366,000.

We use base salaries to recognize the experience, skills, knowledge and responsibilities required of all our employees, including our named executive officers. None of our named executive officers is currently party to an employment agreement or other agreement or arrangement that provides for automatic or scheduled increases in base salary.

Annual Bonus. Our board of directors may, in its discretion, award bonuses to our named executive officers from time to time. Our letter agreements with our named executive officers provide that they will be eligible for annual performance-based bonuses up to a specified percentage of their salary, subject to approval by our board of directors. Performance-based bonuses, which are calculated as a percentage of base salary, are designed to motivate our employees to achieve annual goals based on our strategic, financial and operating performance objectives. From time to time, our board of directors has approved discretionary annual cash bonuses to our named executive officers with respect to their prior year performance.

With respect to 2018 performance, our board of directors awarded bonuses of \$203,734 and \$111,825 to Dr. Gould and Dr. Cadavid, respectively. Because he joined us in December 2018, Mr. Stuart did not receive an annual bonus for 2018.

Equity Incentives. Although we do not have a formal policy with respect to the grant of equity incentive awards to our executive officers, or any formal equity ownership guidelines applicable to them, we believe that equity grants provide our executives with a strong link to our long-term performance, create an ownership culture and help to align the interests of our executives and our stockholders. In addition, we believe that equity grants with a time-based vesting feature promote executive retention because this feature incents our executive officers to remain in our employment during the vesting period. Accordingly, our board of directors periodically reviews the equity incentive compensation of our named executive officers and from time to time may grant equity incentive awards to them in the form of stock options.

Pursuant to their respective letter agreements with us, we granted a restricted stock award for 3,000,000 shares of our common stock to Dr. Gould in July 2016, an option to purchase 2,125,000 shares of our common stock to Mr. Stuart in December 2018, and a restricted stock award for 400,000 shares of our common stock to Dr. Cadavid in October 2016, in each case in connection with the commencement of employment with us. In addition, we granted a restricted stock award for 450,000 shares of our common stock to Dr. Gould in January 2018, a restricted stock award for 60,000 shares of our common stock to Dr. Cadavid in January 2018 and an option to purchase 125,000 shares of our common stock to Dr. Cadavid in July 2018. The equity awards granted in 2018 to Dr. Gould and Dr. Cadavid vest in equal quarterly installments over a term of four years from the applicable vesting commencement date. The options granted in 2018 to Mr. Stuart vest as to 25% of the shares underlying the option on the first anniversary of the vesting commencement date and as to an additional 6.25% of the original number of shares underlying the option quarterly thereafter.

In January 2019, we granted options to purchase 2,422,650, 412,500 and 566,500 shares of our common stock to Dr. Gould, Mr. Stuart and Dr. Cadavid, respectively. The options granted in January 2019 to Dr. Gould and to Dr. Cadavid vest in equal quarterly installments over a term of four years from the vesting commencement date. The options granted in January 2019 to Mr. Stuart vest as to 25% of the shares underlying the option on the first anniversary of the vesting commencement date and as to an additional 6.25% of the original number of shares underlying the option quarterly thereafter. Our board of directors has also granted options to purchase 750,000, 200,000 and 89,490 shares of our common stock to Dr. Gould, Mr. Stuart and Dr. Cadavid, respectively, effective upon the commencement of trading of our

common stock on the Nasdaq Stock Market, which we refer to as the IPO grants. The IPO grants vest in equal quarterly installments over a term of four years from July 1, 2019.

Prior to this offering, our executives were eligible to receive equity awards under our 2016 Stock Incentive Plan, as amended to date, or the 2016 Plan. During 2018 and 2019, all restricted stock awards and stock options (other than the IPO grants) were granted pursuant to the 2016 Plan. Following the closing of this offering, our employees and executives will be eligible to receive stock options and other stock-based awards pursuant to our 2019 Stock Incentive Plan, or the 2019 Plan.

Prior to June 2018, we used restricted stock awards to compensate our executive officers in the form of initial grants in connection with the commencement of employment and also at various times, often but not necessarily annually, if we had performed as expected or better than expected. Since June 2018, we typically use stock options to compensate our executive officers in connection with the commencement of employment and also at various times.

Prior to this offering, awards of restricted stock and stock options to our executive officers have been made by our board of directors. None of our executive officers is currently party to an employment agreement that provides for the automatic award of restricted stock or stock options. We have granted restricted stock and option awards to our executive officers with time-based vesting. The restricted stock and option awards that we have granted to our executive officers in connection with commencement of employment typically become exercisable as to 25% of the shares underlying the award on the first anniversary of the grant date and as to an additional 6.25% of the original number of shares underlying the award quarterly thereafter. The restricted stock and option awards that we have granted to our executive officers at times other than in connection with employment typically become exercisable in equal quarterly installments over a term of four years from the applicable vesting commencement date. Vesting rights cease upon termination of employment and exercise rights for options cease shortly after termination. Prior to the exercise of an option, the holder has no rights as a stockholder with respect to the shares subject to such option, including no voting rights and no right to receive dividends or dividend equivalents.

We have historically granted stock options with exercise prices that are equal to the fair market value of our common stock on the date of grant as determined by our board of directors, based on a number of objective and subjective factors. The exercise price of all stock options granted after the closing of this offering will be equal to the fair market value of shares of our common stock on the date of grant, which will be determined by reference to the closing market price of our common stock on the date of grant.

Outstanding Equity Awards at December 31, 2018

The following table sets forth information regarding all outstanding stock options and restricted stock held by each of our named executive officers as of December 31, 2018.

Name	Option Awards				Stock Awards	
	Number of securities underlying unexercised options (#) exercisable	Number of securities underlying unexercised options (#) unexercisable	Option exercise price (\$)	Option expiration date	Number of shares or units of stock that have not vested (#)	Market value of shares or units of stock that have not vested (\$) ⁽¹⁾
Robert J. Gould	—	—	—	—	1,125,000 ⁽²⁾	—
	—	—	—	—	150,000 ⁽³⁾	—
	—	—	—	—	337,500 ⁽⁴⁾	—
Bryan Stuart	—	2,125,000 ⁽⁵⁾	\$ 1.12	12/17/2028	—	—
Diego Cadavid	7,812	117,188 ⁽⁶⁾	\$ 0.69	7/10/2028	175,000 ⁽⁷⁾	—
					18,750 ⁽⁸⁾	—
					45,000 ⁽⁹⁾	—

- (1) The market price of our common stock is based on an assumed initial public offering price of \$ _____ per share, which is the midpoint of the price range set forth on the cover page of this prospectus.
- (2) Dr. Gould's restricted stock award for 3,000,000 shares vests over four years, with 25% of the shares vested on June 20, 2017, and 6.25% of the original number of shares vesting thereafter in equal quarterly installments through June 20, 2020, subject to continued service.
- (3) Dr. Gould's restricted stock award for 300,000 shares vests over four years, in equal quarterly installments through January 1, 2021, subject to continued service.
- (4) Dr. Gould's restricted stock award for 450,000 shares vests over four years, in equal quarterly installments through January 1, 2022, subject to continued service.
- (5) Mr. Stuart's option award for 2,125,000 shares vests over four years, with 25% of the shares vesting on December 17, 2019, and 6.25% of the original number of shares vesting thereafter in equal quarterly installments through December 17, 2022, subject to continued service.
- (6) Dr. Cadavid's option award for 125,000 shares vests over four years, in equal quarterly installments through July 16, 2022, subject to continued service.
- (7) Dr. Cadavid's restricted stock award for 400,000 shares vests over four years, with 25% of the shares vested on September 19, 2017, and 6.25% of the original number of shares vesting thereafter in equal quarterly installments through September 19, 2020, subject to continued service.
- (8) Dr. Cadavid's restricted stock award for 37,500 shares vests over four years, in equal quarterly installments through January 1, 2021, subject to continued service.
- (9) Dr. Cadavid's restricted stock award for 60,000 shares vests over four years, in equal quarterly installments through January 1, 2022, subject to continued service.

Employment Agreements

Letter Agreement with Robert Gould

In connection with our initial hiring of Dr. Gould as our president and chief executive officer, we entered into a letter agreement with him effective June 13, 2016. Under the letter agreement, Dr. Gould is an at will employee, and his employment with us can be terminated by him or us at any time and for any

reason, provided that Dr. Gould's letter agreement provides that Dr. Gould may terminate his employment voluntarily with us other than for good reason (as defined in the letter agreement) upon at least thirty (30) days' prior written notice to us.

The letter agreement provides that Dr. Gould is entitled to an annualized base salary of \$420,000, and that he is eligible, at our sole discretion, to earn an annual bonus of 35% of his base salary based upon the achievement of corporate and individual goals, as agreed by the board of directors. Dr. Gould's letter agreement also provided that in connection with our consummation of a Series A preferred stock financing, he was entitled to the grant of a restricted stock award for 3,000,000 shares of our common stock, subject to a four-year vesting schedule, which restricted stock award was granted to Dr. Gould in July 2016.

Under the letter agreement, Dr. Gould is entitled, subject to his execution and nonrevocation of a separation agreement and a general release of claims in our favor, in the event of the termination of his employment by us without cause, as defined in his letter agreement with us, to (i) receive 12 months of his then-current annual base salary, payable in equal installments during the six month period following the date his employment with us is terminated, and (ii) our continuing to pay COBRA premiums for health benefit coverage on his behalf, for a period of 12 months following the date his employment with us is terminated, at the same rate as we pay for active employees, subject to applicable COBRA terms and in compliance with applicable non-discrimination or other requirements under the Internal Revenue Code of 1986, as amended, or the Code or the ACA.

Letter Agreement with Bryan Stuart

In connection with our initial hiring of Mr. Stuart as our chief operating officer, we entered into a letter agreement with him effective December 6, 2018. Under the letter agreement, Mr. Stuart is an at will employee, and his employment with us can be terminated by him or us at any time and for any reason.

The letter agreement provides that Mr. Stuart is entitled to an annualized base salary of \$400,000, and that he is eligible, at our sole discretion, to earn an annual bonus of 35% of his base salary based upon the achievement of corporate and individual goals, as agreed by the board of directors. Mr. Stuart's letter agreement also provided that he was entitled to the grant of an option to purchase 2,125,000 shares of our common stock, with an exercise price per share price equal to the fair market value of a share of our common stock on the grant date, subject to a four-year vesting schedule, which option award was granted to Mr. Stuart in December 2018.

Under the letter agreement, Mr. Stuart is entitled, subject to his execution and nonrevocation of a separation agreement and a general release of claims in our favor, in the event of the termination of his employment by us without cause, as defined in his letter agreement with us, to (i) receive six months of his then-current annual base salary, payable in equal installments during the six month period following the date his employment with us is terminated, provided that the first installment shall be made on the 60th day following the date his employment with us is terminated and will include payment of any installment that was otherwise due prior thereto, and (ii) our continuing to pay our share of COBRA premiums for health benefit coverage on his behalf to the same extent we were paying such premiums immediately prior to his termination, for a period of six months following the date that his employment with us is terminated, provided he is eligible for and elects COBRA coverage and continues to pay his share of the COBRA premiums.

Letter Agreement with Diego Cadavid

In connection with our initial hiring of Dr. Cadavid as our vice president, clinical development, we entered into a letter agreement with him effective August 10, 2016. Under the letter agreement,

Dr. Cadavid is an at will employee, and his employment with us can be terminated by him or us at any time and for any reason.

The letter agreement provides that Dr. Cadavid is entitled to an annualized base salary of \$333,000, and that he is eligible, at our sole discretion, to earn an annual bonus of 25% of his base salary based upon the achievement of corporate and individual goals, as agreed by the board of directors. Dr. Cadavid's letter agreement also provided that he was entitled to (i) a \$150,000 cash bonus in connection with the commencement of his employment, of which \$125,000 was paid in September 2016 and \$25,000 was paid in September 2017 and (ii) the grant of a restricted stock award for 400,000 shares of our common stock, with a purchase price per share price equal to the fair market value of a share of our common stock on the grant date, subject to a four-year vesting schedule, which restricted stock award was granted to Dr. Cadavid in October 2016.

Dr. Cadavid was promoted to the position of senior vice president, clinical development on July 16, 2018.

Employee Non-Competition, Non-Solicitation, Confidentiality and Assignment of Inventions Agreements

Each of our named executive officers has entered into a standard form agreement with respect to non-competition, non-solicitation, confidential information and assignment of inventions. In addition, certain of our named executive officers are subject to non-competition restrictions.

Under their respective agreements, each named executive officer has agreed that we own all inventions that are developed by such executive officer during his employment with us that (i) are related to our business or our customers or suppliers or any of our products or services being researched, developed, manufactured or sold by us or which may be used with such products or services, (ii) result from tasks assigned to the executive officer by us or (iii) result from the use of our premises or personal property (whether tangible or intangible) owned, leased or contracted for by us. Each named executive officer also agreed to provide us with a non-exclusive, royalty-free, paid-up, irrevocable, worldwide license for any prior inventions that such executive officer incorporates into any of our products, processes, machines or other works, in the course of such executive officer's employment with us. Under their respective agreements, each of Dr. Gould and Dr. Cadavid has further agreed not to compete with us during his employment and for a period of one year after the termination of his employment, not to solicit our employees, consultants, customers, business or prospective customers during his employment and for a period of one year after the termination of his employment, and to protect our confidential and proprietary information indefinitely. Under his agreement, Mr. Stuart agreed not to solicit our employees, consultants, customers, business or prospective customers during his employment and for a period of one year after the termination of his employment and to protect our confidential and proprietary information indefinitely.

Stock Option and Other Compensation Plans

In this section we describe our 2016 Plan, our 2019 Plan and our 2019 Employee Stock Purchase Plan, or the 2019 ESPP. Prior to this offering, we granted awards to eligible participants under the 2016 Plan. Following the effectiveness of the 2019 Plan, we expect to grant awards to eligible participants from time to time only under the 2019 Plan.

2016 Stock Incentive Plan

The 2016 Plan was initially approved by our board of directors and stockholders in July 2016 and was subsequently amended in 2017, 2018 and 2019, in each case to increase the total number of shares reserved for issuance under the plan. The 2016 Plan provides for the grant of incentive stock options, nonstatutory options, stock appreciation rights, awards of restricted stock, restricted stock units and other stock-based

awards. Our employees, officers, directors, consultants and advisors are eligible to receive awards under the 2016 Plan; however, incentive stock options may only be granted to our employees. The type of award granted under the 2016 Plan and the terms of such award are set forth in the applicable award agreement. Pursuant to the terms of the 2016 Plan, our board of directors (or a committee delegated by our board of directors) administers the plan and, subject to any limitations in the plan, selects the recipients of awards and determines:

- the number of shares of our common stock covered by options and the dates upon which the options become exercisable;
- the type of options to be granted;
- the duration of options, which may not be in excess of ten years;
- the exercise price of options, which must be at least equal to the fair market value of our common stock on the date of grant; and
- the number of shares of our common stock subject to and the terms of any stock appreciation rights, restricted stock awards, restricted stock units or other stock-based awards and the terms and conditions of such awards, including conditions for repurchase, issue price and repurchase price (though the measurement price of stock appreciation rights must be at least equal to the fair market value of our common stock on the date of grant and the duration of such awards may not be in excess of ten years).

The maximum number of shares of common stock authorized for issuance under the 2016 Plan is 24,965,000 shares. Our board of directors may amend, suspend or terminate the 2016 Plan (or any portion of the 2016 Plan) at any time, except that stockholder approval may be required to comply with applicable law.

Effect of Certain Changes in Capitalization

Upon the occurrence of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, spin-off or other similar change in capitalization or event, or any dividend or distribution to holders of our common stock other than an ordinary cash dividend, under the terms of the 2016 Plan, we are required to equitably adjust (or make substitute awards, if applicable), in the manner determined by our board of directors:

- the number and class of securities available under the 2016 Plan;
- the number and class of securities and exercise price per share of each outstanding option;
- the share and per-share provisions and the measurement price of each outstanding stock appreciation right;
- the number of shares subject to and the repurchase price per share subject to each outstanding restricted stock award or restricted stock unit award; and
- the share and per-share-related provisions and the purchase price, if any, of each outstanding other stock-based award.

Effect of Certain Corporate Transactions

Upon the occurrence of a merger or other reorganization event (as defined in the 2016 Plan), our board of directors may, on such terms as our board determines (except to the extent specifically provided otherwise in an applicable award agreement or other agreement between the participant and us), take any

one or more of the following actions pursuant to the 2016 Plan as to all or any (or any portion of) outstanding awards, other than awards of restricted stock:

- provide that outstanding awards will be assumed, or substantially equivalent awards will be substituted, by the acquiring or succeeding corporation (or an affiliate of the acquiring or succeeding corporation);
- upon written notice to a participant, provide that all of the participant's unexercised awards will terminate immediately prior to the consummation of the reorganization event unless exercised by the participant (to the extent then exercisable) within a specified period following the date of the notice;
- provide that outstanding awards will become exercisable, realizable or deliverable, or restrictions applicable to an award will lapse, in whole or in part, prior to or upon such reorganization event;
- in the event of a reorganization event pursuant to which holders of shares of our common stock will receive a cash payment for each share surrendered in the reorganization event, make or provide for a cash payment to participants with respect to each award held by a participant equal to (1) the number of shares of our common stock subject to the vested portion of the award (after giving effect to any acceleration of vesting that occurs upon or immediately prior to the reorganization event) multiplied by (2) the excess, if any, of the cash payment for each share surrendered in the reorganization event over the exercise, measurement or purchase price of such award and any applicable tax withholdings, in exchange for the termination of the award;
- provide that, in connection with our liquidation or dissolution, awards will convert into the right to receive liquidation proceeds (if applicable, net of the exercise measurement or purchase price thereof and any applicable tax withholdings); or
- any combination of the foregoing.

Our board of directors is not obligated under the 2016 Plan to treat all awards, all awards held by a participant, or all awards of the same type, identically.

In the case of certain restricted stock units, no assumption or substitution is permitted, and the restricted stock units will instead be settled in accordance with the terms of the applicable restricted stock unit agreement.

Upon the occurrence of a reorganization event other than our liquidation or dissolution, our repurchase and other rights with respect to outstanding restricted stock awards will continue for the benefit of the succeeding company and will, unless our board of directors determines otherwise, apply to the cash, securities, or other property which our common stock was converted into or exchanged for in the reorganization event in the same manner and to the same extent as they applied to the common stock subject to the restricted stock award. However, the board may provide for the termination or deemed satisfaction of such repurchase or other rights under the restricted stock award agreement or any other agreement between a participant and us, either initially or by amendment. Upon our liquidation or dissolution, except to the extent specifically provided to the contrary in the restricted stock award agreement or any other agreement between the plan participant and us, all restrictions and conditions on all restricted stock awards then outstanding will automatically be deemed terminated or satisfied.

Our board of directors may at any time provide that any award under the 2016 Plan will become immediately exercisable in whole or in part, free of some or all restrictions or conditions, or otherwise realizable in whole or in part, as the case may be.

As of April 30, 2019, there were 11,740,125 shares of restricted common stock outstanding under the 2016 Plan, including 4,040,826 shares of unvested restricted common stock subject to repurchase by us. In addition, as of April 30, 2019, there were options to purchase 10,503,582 shares of common stock outstanding under the 2016 Plan at a weighted average exercise price of \$1.09 per share, options to purchase 195,381 shares of our common stock had been exercised under the 2016 Plan and 2,565,912 shares of common stock were available for future issuance under the 2016 Plan. No further awards will be made under the 2016 Plan on or after the effectiveness of the registration statement for this offering; however, awards outstanding under the 2016 Plan will continue to be governed by their existing terms.

2019 Stock Incentive Plan

We expect our board of directors to adopt and our stockholders to approve the 2019 Plan, which will become effective immediately prior to the effectiveness of the registration statement of which this prospectus forms a part. The 2019 Plan provides for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock units and other stock-based awards. Upon effectiveness of the 2019 Plan, the number of shares of our common stock that will be reserved for issuance under the 2019 Plan will be the sum of: (1) 14,120,000; plus (2) the number of shares (up to 16,569,250 shares) as is equal to the sum of (x) the number of shares of our common stock reserved for issuance under the 2016 Plan that remain available for grant under the 2016 Plan immediately prior to the effectiveness of the registration statement of which this prospectus forms a part and (y) the number of shares of our common stock subject to outstanding awards under the 2016 Plan that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by us at their original issuance price pursuant to a contractual repurchase right; plus (3) an annual increase, to be added on the first day of each fiscal year, beginning with the fiscal year ending December 31, 2020 and continuing until, and including, the fiscal year ending December 31, 2029, equal to the lowest of (i) 14,000,000 shares of our common stock, (ii) 4% of the number of shares of our common stock outstanding on the first day of such fiscal year and (iii) an amount determined by our board of directors.

Our employees, officers, directors, consultants and advisors will be eligible to receive awards under the 2019 Plan. Incentive stock options, however, may only be granted to our employees. Our board of directors has granted under the 2019 Plan options to purchase 2,159,544 shares of our common stock to certain of our employees and non-employee directors effective upon the commencement of trading of our common stock on the Nasdaq Stock Market.

Pursuant to the terms of the 2019 Plan, our board of directors (or a committee delegated by our board of directors) will administer the plan and, subject to any limitations in the plan, will select the recipients of awards and determine:

- the number of shares of our common stock covered by options and the dates upon which the options become exercisable;
- the type of options to be granted;
- the duration of options, which may not be in excess of ten years;
- the exercise price of options, which must be at least equal to the fair market value of our common stock on the date of grant; and
- the number of shares of our common stock subject to and the terms of any stock appreciation rights, restricted stock awards, restricted stock units or other stock-based awards and the terms and conditions of such awards, including conditions for repurchase, issue price and repurchase price (though the measurement price of stock appreciation rights must be at least equal to the fair market value of our common stock on the date of grant and the duration of such awards may not be in excess of ten years).

If our board of directors delegates authority to one or more of our officers to grant awards under the 2019 Plan, the officers will have the power to make awards to all of our employees, except officers and executive officers (as such terms are defined in the 2019 plan). Our board of directors will fix the terms of the awards to be granted by any such officer, the maximum number of shares subject to awards that such officer may make, and the time period in which such awards may be granted.

The 2019 Plan contains limits on awards that may be made under the 2019 Plan to our non-employee directors. In any calendar year, the value (calculated based on grant date fair value for financial reporting purposes) of shares of our common stock subject to awards granted under the 2019 Plan to an individual non-employee director, plus the amount of cash compensation paid to such individual non-employee director may not exceed \$750,000 in the case of an incumbent director, \$1,000,000 in the case of the chairman of our board of directors, or \$1,000,000 in the case of a new director during his or her first year of service. However, our board of directors may make exceptions to this limit for individual non-employee directors in extraordinary circumstances, provided that the non-employee director receiving such additional compensation may not participate in the decision to award such compensation.

Effect of Certain Changes in Capitalization

Upon the occurrence of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, spin-off or other similar change in capitalization or event, or any dividend or distribution to holders of our common stock other than an ordinary cash dividend, under the terms of the 2019 Plan, we are required to equitably adjust (or make substitute awards, if applicable), in the manner determined by our board of directors:

- the number and class of securities available under the 2019 Plan;
- the share counting rules and sublimits of the 2019 Plan;
- the number and class of securities and exercise price per share of each outstanding option;
- the share and per-share provisions and the measurement price of each outstanding stock appreciation right;
- the number of shares subject to, and the repurchase price per share subject to, each outstanding award of restricted stock; and
- the share and per-share related provisions and the purchase price, if any, of each outstanding award of restricted stock units and each other stock-based award.

Effect of Certain Corporate Transactions

Upon the occurrence of a merger or other reorganization event (as defined in the 2019 Plan), our board of directors may, on such terms as our board determines (except to the extent specifically provided otherwise in an applicable award agreement or other agreement between the participant and us), take any one or more of the following actions pursuant to the 2019 Plan as to all or any (or any portion of) outstanding awards, other than awards of restricted stock:

- provide that outstanding awards will be assumed, or substantially equivalent awards will be substituted, by the acquiring or succeeding corporation (or an affiliate of the acquiring or succeeding corporation);
- upon written notice to a participant, provide that all of the participant's unvested awards will be forfeited immediately prior to the consummation of the reorganization event, and/or vested but unexercised awards will terminate immediately prior to the consummation of the reorganization event unless exercised by the participant (to the extent then exercisable) within a specified period following the date of the notice;

- provide that outstanding awards will become exercisable, realizable or deliverable, or restrictions applicable to an award will lapse, in whole or in part, prior to or upon such reorganization event;
- in the event of a reorganization event pursuant to which holders of shares of our common stock will receive a cash payment for each share surrendered in the reorganization event, make or provide for a cash payment to participants with respect to each award held by a participant equal to (1) the number of shares of our common stock subject to the vested portion of the award (after giving effect to any acceleration of vesting that occurs upon or immediately prior to such reorganization event) multiplied by (2) the excess, if any, of the cash payment for each share surrendered in the reorganization event over the exercise, measurement or purchase price of such award and any applicable tax withholdings, in exchange for the termination of such award;
- provide that, in connection with our liquidation or dissolution, awards will convert into the right to receive liquidation proceeds (if applicable, net of the exercise, measurement or purchase price thereof and any applicable tax withholdings); or
- any combination of the foregoing.

Our board of directors is not obligated under the 2019 Plan to treat all awards, all awards held by a participant, or all awards of the same type, identically.

In the case of certain restricted stock units, no assumption or substitution is permitted, and the restricted stock units will instead be settled in accordance with the terms of the applicable restricted stock unit agreement.

Upon the occurrence of a reorganization event other than our liquidation or dissolution, our repurchase and other rights with respect to outstanding awards of restricted stock will continue for the benefit of the succeeding company and will, unless our board of directors determines otherwise, apply to the cash, securities, or other property which our common stock was converted into or exchanged for pursuant to the reorganization event in the same manner and to the same extent as they applied to the common stock subject to the restricted stock award. However, the board may provide for the termination or deemed satisfaction of such repurchase or other rights under the restricted stock award agreement or in any other agreement between a participant and us, either initially or by amendment. Upon our liquidation or dissolution, except to the extent specifically provided to the contrary in the restricted stock award agreement or any other agreement between the participant and us, all restrictions and conditions on all restricted stock awards then outstanding will automatically be deemed terminated or satisfied.

At any time, our board of directors may provide that any award under the 2019 Plan will become immediately exercisable in whole or in part, free of some or all restrictions or conditions, or otherwise realizable in whole or in part as the case may be.

Except with respect to certain actions requiring stockholder approval under the Code or Nasdaq rules, our board of directors may amend, modify or terminate any outstanding award under the 2019 Plan, including but not limited to, substituting for the award another award of the same or a different type, changing the date of exercise or realization, and converting an incentive stock option to a nonstatutory stock option, subject to certain participant consent requirements. However, unless our stockholders approve such action, the 2019 Plan provides that we may not (except as otherwise permitted in connection with a change in capitalization or reorganization event):

- amend any outstanding stock option or stock appreciation right granted under the 2019 Plan to provide an exercise or measurement price per share that is lower than the then-current exercise or measurement price per share of such outstanding award;
- cancel any outstanding stock option or stock appreciation right (whether or not granted under the 2019 Plan) and grant a new award under the 2019 Plan in substitution for the cancelled award (other than substitute awards permitted in connection with a merger or consolidation of an entity

with us or our acquisition of property or stock of another entity) covering the same or a different number of shares of our common stock and having an exercise or measurement price per share lower than the then-current exercise or measurement price per share of the cancelled award;

- cancel in exchange for a cash payment any outstanding option or stock appreciation right with an exercise or measurement price per share above the then-current fair market value of our common stock (valued in the manner determined by (or in the manner approved by) our board of directors); or
- take any other action that constitutes a "repricing" within the meaning of Nasdaq rules or rules of any other exchange or marketplace on which our common stock is listed or traded.

No award may be granted under the 2019 Plan on or after the date that is ten years following the effectiveness of the registration statement related to this offering. Our board of directors may amend, suspend or terminate the 2019 Plan at any time, except that stockholder approval may be required to comply with applicable law or stock market requirements.

2019 Employee Stock Purchase Plan

We expect our board of directors to adopt and our stockholders to approve the 2019 ESPP, which will become effective immediately prior to the effectiveness of the registration statement of which this prospectus forms a part. The 2019 ESPP will be administered by our board of directors or by a committee appointed by our board of directors. The 2019 ESPP initially provides participating employees with the opportunity to purchase up to an aggregate of 1,765,000 shares of our common stock. The number of shares of our common stock reserved for issuance under the 2019 ESPP will automatically increase on the first day of each fiscal year, beginning with the fiscal year ending on December 31, 2020 and continuing until, and including, the fiscal year ending on December 31, 2029, in an amount equal to the lowest of (i) 3,000,000 shares of our common stock, (ii) 1% of the number of shares of our common stock outstanding on such date and (iii) an amount determined by our board of directors.

All of our employees and employees of any designated subsidiary, as defined in the 2019 ESPP, are eligible to participate in the 2019 ESPP, provided that:

- such person is customarily employed by us or a designated subsidiary for more than 20 hours a week and for more than five months in a calendar year;
- such person has been employed by us or by a designated subsidiary for at least three months prior to enrolling in the 2019 ESPP; and
- such person was our employee or an employee of a designated subsidiary on the first day of the applicable offering period under the 2019 ESPP.

We retain the discretion to determine which eligible employees may participate in an offering under applicable regulations.

We expect to make one or more offerings to our eligible employees to purchase stock under the 2019 ESPP beginning at such time and on such dates as our board of directors may determine, or on the first business day thereafter. Each offering will consist of a six-month offering period during which payroll deductions will be made and held for the purchase of our common stock at the end of the offering period. Our board of directors or a committee designated by the board of directors may, at its discretion, choose a different period of not more than 12 months for offerings.

On each offering commencement date, each participant will be granted an option to purchase, on the last business day of the offering period, up to a number of shares of our common stock determined by multiplying \$2,083 by the number of full months in the offering period and dividing that product by the closing price of our common stock on the first day of the offering period. No employee may be granted an

option under the 2019 ESPP that permits the employee's rights to purchase shares under the 2019 ESPP and any other employee stock purchase plan of ours or of any of our subsidiaries to accrue at a rate that exceeds \$25,000 of the fair market value of our common stock (determined as of the first day of each offering period) for each calendar year in which the option is outstanding. In addition, no employee may purchase shares of our common stock under the 2019 ESPP that would result in the employee owning 5% or more of the total combined voting power or value of our stock or the stock of any of our subsidiaries.

On the commencement date of each offering period, each eligible employee may authorize up to a maximum of 15% of his or her compensation to be deducted by us during the offering period. Each employee who continues to be a participant in the 2019 ESPP on the last business day of the offering period will be deemed to have exercised an option to purchase from us the number of whole shares of our common stock that his or her accumulated payroll deductions on such date will pay for, not in excess of the maximum numbers set forth above. Under the terms of the 2019 ESPP, the purchase price will be determined by our board of directors or the committee for each offering period and will be at least 85% of the applicable closing price of our common stock. If our board of directors or the committee does not make a determination of the purchase price, the purchase price will be 85% of the lesser of the closing price of our common stock on the first business day of the offering period or on the last business day of the offering period.

An employee may at any time prior to the close of business on the fifteenth business day (or such other number of days as is determined by us) prior to the end of the offering period, and for any reason, permanently withdraw from participating in the offering and permanently withdraw the balance accumulated in the employee's account. If an employee elects to discontinue his or her payroll deductions during an offering period but does not elect to withdraw his or her funds, funds previously deducted will be applied to the purchase of common stock at the end of the offering period. If a participating employee's employment ends before the last business day of an offering period, no additional payroll deductions will be taken and the balance in the employee's account will be paid to the employee.

We will be required to make equitable adjustments to the extent determined by our board of directors or a committee thereof to the number and class of securities available under the 2019 ESPP, the share limitations under the 2019 ESPP, and the purchase price for an offering period under the 2019 ESPP to reflect stock splits, reverse stock splits, stock dividends, recapitalizations, combinations of shares, reclassifications of shares, spin-offs and other similar changes in capitalization or events or any dividends or distributions to holders of our common stock other than ordinary cash dividends.

In connection with a merger or other reorganization event, as defined in the 2019 ESPP, our board of directors or a committee of our board of directors may take any one or more of the following actions as to outstanding options to purchase shares of our common stock under the 2019 ESPP on such terms as our board of directors or committee thereof determines:

- provide that options will be assumed, or substantially equivalent options will be substituted, by the acquiring or succeeding corporation (or an affiliate of the acquiring or succeeding corporation);
- upon written notice to employees, provide that all outstanding options will be terminated immediately prior to the consummation of such reorganization event and that all such outstanding options will become exercisable to the extent of accumulated payroll deductions as of a date specified by board of directors or committee thereof in such notice, which date will not be less than ten days preceding the effective date of the reorganization event;
- upon written notice to employees, provide that all outstanding options will be cancelled as of a date prior to the effective date of the reorganization event and that all accumulated payroll deductions will be returned to participating employees on such date;
- in the event of a reorganization event under the terms of which holders of our common stock will receive upon consummation thereof a cash payment for each share surrendered in the

reorganization event, change the last day of the offering period to be the date of the consummation of the reorganization event and make or provide for a cash payment to each employee equal to (1) the cash payment for each share surrendered in the reorganization event times the number of shares of our common stock that the employee's accumulated payroll deductions as of immediately prior to the reorganization event could purchase at the applicable purchase price, where the cash payment for each share surrendered in the reorganization event is treated as the fair market value of our common stock on the last day of the applicable offering period for purposes of determining the purchase price and where the number of shares that could be purchased is subject to the applicable limitations under the 2019 ESPP minus (2) the result of multiplying such number of shares by the purchase price; and/or

- provide that, in connection with our liquidation or dissolution, options will convert into the right to receive liquidation proceeds (net of the purchase price thereof).

Our board of directors may at any time, and from time to time, amend or suspend the 2019 ESPP or any portion of the 2019 ESPP. We will obtain stockholder approval for any amendment if such approval is required by Section 423 of the Code. Further, our board of directors may not make any amendment that would cause the 2019 ESPP to fail to comply with Section 423 of the Internal Revenue Code. The 2019 ESPP may be terminated at any time by our board of directors. Upon termination, we will refund all amounts in the accounts of participating employees.

401(k) Plan

We maintain a defined contribution employee retirement plan for our employees, including our named executive officers. The plan is intended to qualify as a tax-qualified 401(k) plan so that contributions to the 401(k) plan, and income earned on such contributions, are not taxable to participants until withdrawn or distributed from the 401(k) plan (except in the case of contributions under the 401(k) plan designated as Roth contributions). Under the 401(k) plan, each employee is fully vested in his or her deferred salary contributions and our discretionary match. Employee contributions are held and invested by the plan's trustee as directed by participants. The 401(k) plan provides us with the discretion to match employee contributions, but to date we have not provided any employer matching contributions.

Limitation of Liability and Indemnification

Our certificate of incorporation, which will become effective upon the closing of this offering, limits the personal liability of directors for breach of fiduciary duty to the maximum extent permitted by the Delaware General Corporation Law, or the DGCL, and provides that no director will have personal liability to us or to our stockholders for monetary damages for breach of fiduciary duty as a director. However, these provisions do not eliminate or limit the liability of any of our directors:

- for any breach of the director's duty of loyalty to us or our stockholders;
- for acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;
- for voting for or assenting to unlawful payments of dividends, stock repurchases or other distributions; or
- for any transaction from which the director derived an improper personal benefit.

Any amendment to or repeal of these provisions will not eliminate or reduce the effect of these provisions in respect of any act, omission or claim that occurred or arose prior to such amendment or repeal. If the DGCL is amended to provide for further limitations on the personal liability of directors of corporations, then the personal liability of our directors will be further limited to the greatest extent permitted by the DGCL.

In addition, our certificate of incorporation, which will become effective upon the closing of this offering, provides that we must indemnify our directors and officers and we must advance expenses, including attorneys' fees, to our directors and officers in connection with legal proceedings, subject to very limited exceptions.

We maintain a general liability insurance policy that covers specified liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers. In addition, we intend to enter into indemnification agreements with all of our executive officers and directors prior to the completion of this offering. These indemnification agreements may require us, among other things, to indemnify each such executive officer or director for some expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by him or her in any action or proceeding arising out of his or her service as one of our executive officers or directors.

Some of our non-employee directors may, through their relationships with their employers, be insured or indemnified against specified liabilities incurred in their capacities as members of our board of directors.

Insofar as indemnification for liabilities arising under the Securities Act of 1933, or the Securities Act, may be permitted to directors, executive officers or persons controlling us, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

Rule 10b5-1 Sales Plans

Our directors and executive officers may adopt written plans, known as Rule 10b5-1 plans, in which they will contract with a broker to buy or sell shares of our common stock on a periodic basis. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the director or officer when entering into the plan, without further direction from the director or officer. It also is possible that the director or officer could amend or terminate the plan when not in possession of material, nonpublic information. In addition, our directors and executive officers may buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material, nonpublic information.

Director Compensation

The table below shows all compensation to our non-employee directors during the year ended December 31, 2018.

<u>Name</u>	<u>Fees earned or paid in cash (\$)</u>	<u>Stock awards (\$)⁽¹⁾</u>	<u>Option awards (\$)⁽²⁾⁽³⁾</u>	<u>Total (\$)</u>
James J. Collins	35,000	—	11,576	46,576
Alan Ezekowitz	35,000	—	11,549	46,549
James Geraghty	35,000	—	11,480	46,480
Kate Haviland ⁽⁴⁾	17,500	—	82,459	99,959
Mark Levin	—	—	—	—
James Tananbaum ⁽⁵⁾	—	—	—	—

(1) As of December 31, 2018, the aggregate number of shares of our common stock held pursuant to restricted stock awards by each non-employee director was as follows: Dr. Collins, 165,000 shares; Mr. Ezekowitz, 165,000 shares; Mr. Geraghty, 565,000 shares; Ms. Haviland, 0 shares; Mr. Levin, 0 shares and Mr. Tananbaum, 0 shares.

(2) The amounts reported in the "Option awards" column reflect the aggregate fair value of stock-based compensation awarded during the year computed in accordance with the provisions of ASC 718. See Note 8 to our consolidated financial statements appearing at the end of this prospectus regarding

assumptions underlying the valuation of equity awards. These amounts reflect the accounting cost for these stock options and do not reflect the actual economic value that may be realized by the directors upon the vesting of the stock options, the exercise of the stock options or the sale of the common underlying such stock options.

- (3) As of December 31, 2018, the aggregate number of shares of our common stock subject to outstanding option awards for each non-employee director was as follows: Dr. Collins, 25,000 shares; Mr. Ezekowitz, 25,000 shares; Mr. Geraghty, 25,000 shares; Ms. Haviland, 165,000 shares; Mr. Levin, 0 shares and Mr. Tananbaum, 0 shares.
- (4) Kate Haviland joined our board of directors in June 2018.
- (5) James Tananbaum resigned from our board of directors effective as of April 3, 2019.

In January 2019, Mr. Collins and Mr. Ezekowitz were each granted options to purchase 25,000 shares of our common stock. In May 2019, Mr. Geraghty was granted an option to purchase 25,000 shares of our common stock. Our board of directors has also granted an option to purchase 65,000 shares of our common stock to each of Mr. Geraghty and Ms. Haviland and an option to purchase 40,000 shares of our common stock to each of Dr. Collins and Mr. Ezekowitz, in each case effective upon the commencement of trading of our common stock on the Nasdaq Stock Market.

Prior to this offering, we paid cash fees and granted restricted stock awards and options to purchase shares of our common stock to certain of our non-employee directors for their service on our board of directors pursuant to a non-employee and non-affiliate director compensation policy. We have historically reimbursed our non-employee directors for reasonable travel and out-of-pocket expenses incurred in connection with attending board of director and committee meetings.

Dr. Gould, one of our directors who also serves as our president and chief executive officer, does not receive any additional compensation for his service as a director. Dr. Gould is one of our named executive officers and, accordingly, the compensation that we pay to Dr. Gould is discussed above under "—Summary Compensation Table" and "—Narrative to Summary Compensation Table."

In June 2019, our board of directors approved a director compensation program that will become effective on the effective date of the registration statements of which this prospectus is a part. Under this director compensation program, we will pay our non-employee directors a cash retainer for service on the board of directors and for service on each committee on which the director is a member. The chairman of the board and of each committee will receive additional retainers for such service. These fees are payable in arrears in four equal quarterly installments on the last day of each quarter, provided that the amount of such payment will be prorated for any portion of such quarter that the director is not serving on our board of directors and no fee will be payable in respect of any period prior to the completion of this offering. The fees paid to non-employee directors for service on the board of directors and for service on each committee of the board of directors on which the director is a member are as follows:

	Member Annual Fee	Chairman Supplemental Annual Fee
Board of Directors	\$ 35,000	\$ 30,000
Audit Committee	\$ 7,500	\$ 7,500
Compensation Committee	\$ 5,000	\$ 5,000
Nominating and Corporate Governance Committee	\$ 4,000	\$ 4,000

We also will continue to reimburse our non-employee directors for reasonable travel and other expenses incurred in connection with attending meetings of our board of directors and any committee of our board of directors on which he or she serves.

In addition, under our director compensation program to be effective on the effective date of the registration statement of which this prospectus is a part, each non-employee director will receive, upon his or her initial election or appointment to our board of directors, an option to purchase 130,000 shares of our common stock under the 2019 Plan. Each of these options will vest as to 2.7778% of the shares of our common stock underlying such option at the end of each successive one month period following the grant date until the third anniversary of the grant date, subject to the non-employee director's continued service as a director. Further, on the date of the first board meeting held after each annual meeting of stockholders, each non-employee director that has served on our board of directors for at least six months will receive, under the 2019 Plan, an option to purchase 65,000 shares of our common stock under the 2019 Plan. Each of these options will vest with respect to all of the shares underlying such option on the first anniversary of the grant date or, if earlier, immediately prior to the first annual meeting of stockholders occurring after the grant date, subject to the non-employee director's continued service as a director. All options issued to our non-employee directors under our director compensation program will be issued at exercise prices equal to the fair market value of our common stock on the date of grant and will become exercisable in full upon specified change in control events.

TRANSACTIONS WITH RELATED PERSONS

Since January 1, 2016, we have engaged in the following transactions in which the amounts involved exceeded \$120,000 and any of our directors, executive officers or holders of more than 5% of our voting securities, or any member of the immediate family of, or person sharing the household with, the foregoing persons, had or will have a direct or indirect material interest. We believe that all of these transactions were on terms as favorable as could have been obtained from unrelated third parties.

Convertible Promissory Note

On April 14, 2016, we issued and sold a convertible promissory note to Third Rock Ventures III, L.P. in the aggregate principal amount of \$3,500,000. The note accrued interest at a rate of 6% per annum. All principal and interest under the note was converted into shares of Series A preferred stock in connection with our initial closing of our Series A preferred stock financing in July 2016.

Series A Preferred Stock Financing

From July 18, 2016 to June 6, 2018, we issued and sold an aggregate of 60,000,000 shares of our Series A preferred stock, consisting of (i) 53,313,014 shares sold at a price per share of \$1.00 in cash, for an aggregate purchase price of \$53,313,014 and (ii) 6,686,986 shares issued upon conversion of \$6,868,986 in outstanding principal and accrued and unpaid interest under the notes issued on October 15, 2015 and April 14, 2016, at a price per share of \$1.00 in cash. The following table sets forth the aggregate numbers of shares of our Series A preferred stock that we issued and sold to our 5% stockholders and their affiliates in this transaction and the aggregate amount of consideration for such shares:

<u>Purchaser⁽¹⁾⁽²⁾</u>	<u>Date</u>	<u>Shares of Series A Preferred Stock Sold for Cash</u>	<u>Cash Purchase Price</u>	<u>Shares of Series A Preferred Stock Received upon Conversion of Promissory Note</u>	<u>Purchase Price Funded by Conversion of Promissory Note</u>
Third Rock Ventures III, L.P.	7/18/2016	5,156,507	\$ 5,156,507	6,686,986	\$ 6,686,986
Third Rock Ventures III, L.P.	11/15/2016	5,156,507	\$ 5,156,507	—	—
Third Rock Ventures III, L.P.	2/17/2017	6,333,333	\$ 6,333,333	—	—
Third Rock Ventures III, L.P.	5/3/2017	3,166,667	\$ 3,166,667	—	—
Third Rock Ventures IV, L.P.	5/3/2017	3,166,666	\$ 3,166,666	—	—
Third Rock Ventures III, L.P.	1/4/2018	3,166,667	\$ 3,166,667	—	—
Third Rock Ventures IV, L.P.	1/4/2018	3,166,667	\$ 3,166,667	—	—
Third Rock Ventures III, L.P.	3/13/2018	3,166,667	\$ 3,166,667	—	—
Third Rock Ventures IV, L.P.	3/13/2018	3,166,666	\$ 3,166,666	—	—
Third Rock Ventures III, L.P.	5/9/2018	3,166,666	\$ 3,166,666	—	—
Third Rock Ventures IV, L.P.	5/9/2018	3,166,667	\$ 3,166,667	—	—
Third Rock Ventures III, L.P.	6/6/2018	3,166,667	\$ 3,166,667	—	—
Third Rock Ventures IV, L.P.	6/6/2018	3,166,667	\$ 3,166,667	—	—

(1) See "Principal Stockholders" for additional information about shares held by these entities.

(2) Mr. Levin, a member of our board of directors, is a partner of Third Rock Ventures.

Series B Preferred Stock Financing

In August 2018, we issued and sold an aggregate of 40,000,000 shares of our Series B preferred stock at a price per share of \$2.00 in cash, for an aggregate purchase price of \$80,000,000. The following table sets forth the aggregate numbers of shares of our Series B preferred stock that we sold to our 5%

stockholders and their affiliates in this transaction and the aggregate amount of consideration for such shares:

<u>Purchaser⁽¹⁾</u>	<u>Shares of Series B Preferred Stock</u>	<u>Cash Purchase Price</u>
Foresite Capital Fund IV, L.P. ⁽²⁾	10,500,000	\$ 21,000,000

- (1) See "Principal Stockholders" for additional information about shares held by these entities.
- (2) Mr. Tananbaum, a former member of our board of directors who served during this transaction, is founder and chief executive officer of Foresite Capital Management.

Agreement with GSK

On February 8, 2019, we entered into a right of reference and license agreement with affiliates of GlaxoSmithKline plc, or GSK, pursuant to which GSK granted us a right of reference to certain INDs filed with the FDA and controlled by GSK or its affiliates relating to losmapimod and an exclusive worldwide license under certain patent rights related to losmapimod. The agreement also provides us with an exclusive worldwide license to certain of GSK's preclinical and clinical data with respect to losmapimod. As partial consideration for the right of reference and licenses granted under the agreement, we issued 12,500,000 shares of our Series B preferred stock to GSK at the time we entered into the right of reference and license agreement.

We also agreed to provide GSK the opportunity to purchase shares of common stock in connection with this offering equal to the proportion that the shares of common stock held by GSK (assuming conversion of all preferred stock into common stock upon consummation of this offering) bear to the total number of shares of common stock immediately prior to the closing of this offering (assuming conversion of all preferred stock into common stock upon consummation of this offering and all outstanding options). If GSK exercises its rights to purchase shares of common stock in connection with this offering, subject to certain conditions, GSK may purchase shares offered in this offering or may purchase shares of common stock in a private placement that is expected to close concurrently with this offering, in each case at the initial per share public offering price.

See "Business—Right of Reference and License Agreement with GlaxoSmithKline" for additional information regarding this agreement.

Consulting Services Provided by Third Rock Ventures, LLC

Since inception, we have received consulting and management services from Third Rock Ventures LLC, or Third Rock Ventures, which through its affiliates, has a significant interest in us. We have paid Third Rock Ventures \$1.9 million for these services since January 1, 2016, including the reimbursement of expenses. We do not have a written agreement in place with Third Rock Ventures with respect to the provision of consulting and management services. The consulting and management services fees are payable to Third Rock Ventures pursuant to invoices submitted to us by Third Rock Ventures quarterly. The consulting and management services fees paid to Third Rock Ventures did not exceed 5% of the consolidated gross revenue of Third Rock Ventures during any of the past three fiscal years. From time to time and at our request, partners and associates of Third Rock Ventures provide us with certain strategic and ordinary course business operations consulting services. We have issued an aggregate of 996,000 shares of our common stock to these consultants in exchange for their continuing consulting services. We may continue to occasionally engage Third Rock Ventures or their partners or associates for consulting services following this offering.

Registration Rights

We are a party to an investor rights agreement with the holders of our preferred stock, including our 5% stockholders and their affiliates and entities affiliated with some of our directors. This investor rights agreement provides these holders the right, subject to certain conditions, beginning six months following the completion of this offering, to demand that we file a registration statement or to request that their shares be covered by a registration statement that we are otherwise filing.

See "Description of Capital Stock—Registration Rights" for additional information regarding these registration rights.

Indemnification Agreements

Our certificate of incorporation, which will become effective upon the closing of this offering, provides that we will indemnify our directors and officers to the fullest extent permitted by Delaware law. In addition, we intend to enter into indemnification agreements with all of our directors and executive officers prior to the completion of this offering. These indemnification agreements may require us, among other things, to indemnify each such director or executive officer for some expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by him or her in any action or proceeding arising out of his or her service as one of our directors or executive officers.

Policies and Procedures for Related Person Transactions

Our board of directors has adopted written policies and procedures, which will be effective at the time of this offering, for the review of any transaction, arrangement or relationship in which our company is a participant, the amount involved exceeds \$120,000 and one of our executive officers, directors, director nominees or 5% stockholders, or their immediate family members, each of whom we refer to as a "related person," has a direct or indirect material interest.

If a related person proposes to enter into such a transaction, arrangement or relationship, which we refer to as a "related person transaction," the related person must report the proposed related person transaction to our general counsel, and if none, our chief operating officer or chief financial officer. The policy calls for the proposed related person transaction to be reviewed and, if deemed appropriate, approved by our audit committee. Whenever practicable, the reporting, review and approval will occur prior to entry into the transaction. If advance review and approval is not practicable, the audit committee will review, and, in its discretion, may ratify the related person transaction. The policy also permits the chairman of the audit committee to review and, if deemed appropriate, approve proposed related person transactions that arise between committee meetings, subject to ratification by the committee at its next meeting. Any related person transactions that are ongoing in nature will be reviewed annually.

A related person transaction reviewed under the policy will be considered approved or ratified if it is authorized by the audit committee after full disclosure of the related person's interest in the transaction. As appropriate for the circumstances, the audit committee will review and consider:

- the related person's interest in the related person transaction;
- the approximate dollar value of the amount involved in the related person transaction;
- the approximate dollar value of the amount of the related person's interest in the transaction without regard to the amount of any profit or loss;
- whether the transaction was undertaken in the ordinary course of our business;
- whether the terms of the transaction are no less favorable to us than terms that could have been reached with an unrelated third party;
- the purpose of, and the potential benefits to us of, the transaction; and

- any other information regarding the related person transaction or the related person in the context of the proposed transaction that would be material to investors in light of the circumstances of the particular transaction.

Our audit committee may approve or ratify the transaction only if it determines that, under all of the circumstances, the transaction is in, or is not inconsistent with, our best interests. Our audit committee may impose any conditions on the related person transaction that it deems appropriate.

In addition to the transactions that are excluded by the instructions to the SEC's related person transaction disclosure rule, our board of directors has determined that the following transactions do not create a material direct or indirect interest on behalf of related persons and, therefore, are not related person transactions for purposes of this policy:

- interests arising solely from the related person's position as an executive officer of another entity, whether or not the person is also a director of the entity, that is a participant in the transaction where the related person and all other related persons own in the aggregate less than a 10% equity interest in such entity, the related person and his or her immediate family members are not involved in the negotiation of the terms of the transaction and do not receive any special benefits as a result of the transaction and the amount involved in the transaction is less than the greater of \$200,000 or 5% of the annual gross revenues of the company receiving payment under the transaction; and
- a transaction that is specifically contemplated by provisions of our certificate of incorporation or bylaws.

The policy provides that transactions involving compensation of executive officers shall be reviewed and approved by our compensation committee in the manner specified in the compensation committee's charter.

We did not have a written policy regarding the review and approval of related person transactions prior to this offering. Nevertheless, with respect to such transactions, it has been the practice of our board of directors to consider the nature of and business reasons for such transactions, how the terms of such transactions compared to those which might be obtained from unaffiliated third parties and whether such transactions were otherwise fair to and in the best interests of, or not contrary to, our best interests.

PRINCIPAL STOCKHOLDERS

The following table sets forth information with respect to the beneficial ownership of our common stock as of April 30, 2019 by:

- each of our directors;
- each of our named executive officers;
- all of our directors and executive officers as a group; and
- each person, or group of affiliated persons, who is known by us to beneficially own more than 5% of our common stock.

The column entitled "Percentage of Shares Beneficially Owned—Before Offering" is based on a total of 131,930,506 shares of our common stock outstanding as of April 30, 2019, assuming the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 112,500,000 shares of our common stock upon the closing of this offering. The column entitled "Percentage of Shares Beneficially Owned—After Offering" is based on shares of our common stock to be outstanding after this offering, including the shares of our common stock that we are selling in this offering, but not including any additional shares issuable upon exercise of outstanding options.

Beneficial ownership is determined in accordance with the rules and regulations of the SEC and includes voting or investment power with respect to our common stock. Shares of our common stock subject to options that are currently exercisable or exercisable within 60 days after April 30, 2019 are considered outstanding and beneficially owned by the person holding the options for the purpose of calculating the percentage ownership of that person but not for the purpose of calculating the percentage ownership of any other person. Except as otherwise noted, the persons and entities in this table have sole voting and investing power with respect to all of the shares of our common stock beneficially owned by them, subject to community property laws, where applicable. Except as otherwise set forth below, the address of each beneficial owner is c/o Fulcrum Therapeutics, Inc., 26 Landsdowne Street, Cambridge, MA 02139.

<u>Name and Address of Beneficial Owner</u>	<u>Number of Shares Beneficially Owned</u>	<u>Percentage of Shares Beneficially Owned</u>	
		<u>Before Offering (%)</u>	<u>After Offering (%)</u>
5% Stockholders			
Entities affiliated with Third Rock Ventures ⁽¹⁾	57,000,000	43.2	
Glaxo Group Limited ⁽²⁾	12,500,000	9.5	
Foresite Capital Fund IV, L.P. ⁽³⁾	10,500,000	8.0	
Directors and Named Executive Officers			
Robert J. Gould ⁽⁴⁾	3,901,415	3.0	
Bryan Stuart	—	*	
Diego Cadavid ⁽⁵⁾	556,343	*	
Mark Levin ⁽⁶⁾	41,166,667	31.2	
James J. Collins ⁽⁷⁾	196,250	*	
Alan Ezekowitz ⁽⁸⁾	202,500	*	
James Geraghty ⁽⁹⁾	590,000	*	
Kate Haviland ⁽¹⁰⁾	41,250	*	
All current executive officers and directors as a group (9 persons) ⁽¹¹⁾	47,544,044	36.0	

* Less than one percent

- (1) Consists of (i) (a) 2,000,000 shares of common stock and (b) 39,166,667 shares of common stock issuable upon the conversion of preferred stock held by Third Rock Ventures III, L.P., or TRV III LP, and (ii) 15,833,333 shares of common stock issuable upon the conversion of preferred stock held by Third Rock Ventures IV, L.P., or TRV IV LP. Third Rock Ventures GP III, L.P., or TRV GP III, is the sole general partner of TRV III LP. TRV GP III, LLC, or TRV III LLC, is the sole general partner of TRV GP III. Each of TRV GP III, TRV III LLC, and Mark Levin, Kevin Starr and Robert Tepper, the managers of TRV III LLC, may be deemed to share voting and dispositive power over the shares of record held by TRV III LP. Each of TRV GP III, TRV III LLC, and Mark Levin, Kevin Starr and Robert Tepper disclaims beneficial ownership of all shares held by TRV III LP except to the extent of their pecuniary interest therein. Third Rock Ventures GP IV, L.P., or TRV GP IV, is the sole general partner of TRV IV LP. TRV GP IV, LLC, or TRV IV LLC, is the sole general partner of TRV GP IV. Abbie Celniker, Ph.D., Robert Tepper, M.D., Craig Muir and Cary Pfeffer, M.D. are the managing members of TRV IV LLC who collectively make voting and investment decisions with respect to shares held by TRV IV LP. The address of TRV III LP and TRV IV LP is 29 Newbury Street, Boston, MA 02116.
- (2) Consists of 12,500,000 shares of common stock issuable upon the conversion of preferred stock held by Glaxo Group Limited, an indirect wholly-owned subsidiary of GlaxoSmithKline plc, which beneficially owns the shares held by Glaxo Group Limited. The address of Glaxo Group Limited is 980 Great West Road, Brentford, Middlesex TW8 9GS England.
- (3) Consists of 10,500,000 shares of common stock issuable upon the conversion of preferred stock held by Foresite Capital Fund, IV, L.P., or FCF IV. Foresite Capital Management IV, LLC, or FCM IV, the general partner of FCF IV, may be deemed to have sole voting and dispositive power over these shares. James B. Tananbaum, in his capacity as managing member of FCM IV, may be deemed to have sole voting and dispositive power over these shares. Each of FCM IV and its members and Mr. Tananbaum disclaims beneficial ownership of any of these shares except to the extent of any pecuniary interest therein. The address of FCF IV is 600 Montgomery Street, Suite 4500, San Francisco, CA 94111.
- (4) Consists of 3,901,415 shares of common stock held by Dr. Gould.
- (5) Consists of 497,500 shares of common stock held by Dr. Cadavid and 58,843 shares of common stock underlying options held by Dr. Cadavid that are exercisable as of April 30, 2019 or will become exercisable within 60 days after such date.
- (6) Consists of the shares described in Note 1 above held by TRV III LP. Mr. Levin, a member of our board of directors, is a manager of TRV III LLC, which is the sole general partner of TRV GP III, which is the sole general partner of TRV III LP and may be deemed to be the indirect beneficial owner of such shares. Mr. Levin disclaims beneficial ownership over such shares, except to the extent of his proportionate pecuniary interest therein.
- (7) Consists of 165,000 shares of common stock held by Dr. Collins and 31,250 shares of common stock underlying options held by Dr. Collins that are exercisable as of April 30, 2019 or will become exercisable within 60 days after such date.
- (8) Consists of 165,000 shares of common stock held by Dr. Ezekowitz and 37,500 shares of common stock underlying options held by Dr. Ezekowitz that are exercisable as of April 30, 2019 or will become exercisable within 60 days after such date.
- (9) Consists of 565,000 shares of common stock held by Mr. Geraghty and 25,000 shares of common stock underlying options held by Mr. Geraghty that are exercisable as of April 30, 2019 or will become exercisable within 60 days after such date.
- (10) Consists of 41,250 shares of common stock underlying options held by Ms. Haviland that are exercisable as of April 30, 2019 or will become exercisable within 60 days after such date.
- (11) Includes 193,843 shares of common stock underlying options that are exercisable as of April 30, 2019 or will become exercisable within 60 days after such date.

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock and provisions of our certificate of incorporation and bylaws are summaries and are qualified by reference to the certificate of incorporation and the bylaws that will be in effect upon the closing of this offering. We will file copies of these documents with the SEC as exhibits to our registration statement of which this prospectus is a part. The description of the capital stock reflects changes to our capital structure that will occur upon the closing of this offering.

Upon the closing of this offering, our authorized capital stock will consist of 200,000,000 shares of our common stock, par value \$0.001 per share, and 5,000,000 shares of our preferred stock, par value \$0.001 per share, all of which preferred stock will be undesignated.

As of April 30, 2019, we had issued and outstanding:

- 19,430,506 shares of our common stock held by 77 stockholders of record;
- 60,000,000 shares of our Series A preferred stock held by 3 stockholders of record, convertible into 60,000,000 shares of our common stock; and
- 52,500,000 shares of our Series B preferred stock held by 21 stockholders of record, convertible into 52,500,000 shares of our common stock;

Upon the closing of this offering, all of the outstanding shares of our preferred stock will automatically convert into an aggregate of 112,500,000 shares of our common stock.

Common Stock

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. Each election of directors by our stockholders will be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights of outstanding preferred stock.

In the event of our liquidation or dissolution, the holders of our common stock are entitled to receive proportionately all assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any of our outstanding preferred stock. Holders of our common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of holders of our common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of our preferred stock that we may designate and issue in the future.

Preferred Stock

Under the terms of our certificate of incorporation that will become effective upon the closing of this offering, our board of directors is authorized to issue shares of preferred stock in one or more series without stockholder approval. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock.

The purpose of authorizing our board of directors to issue preferred stock and determine its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions, future financings and other corporate purposes, could have the effect of making it more difficult for a third party to acquire, or could discourage a third party from seeking to acquire, a majority of our outstanding voting stock. Upon the closing of this offering, there will be no shares of preferred stock outstanding, and we have no present plans to issue any shares of preferred stock.

Options and Unvested Restricted Stock

As of April 30, 2019, options to purchase an aggregate of 10,503,582 shares of our common stock, at a weighted average exercise price of \$1.09 per share, were outstanding, and 6,972,076 shares of unvested restricted common stock were outstanding.

Delaware Anti-Takeover Law and Certain Charter and Bylaw Provisions

Delaware Law

We are subject to Section 203 of the DGCL. Subject to certain exceptions, Section 203 prevents a publicly held Delaware corporation from engaging in a "business combination" with any "interested stockholder" for three years following the date that the person became an interested stockholder, unless either the interested stockholder attained such status with the approval of our board of directors, the business combination is approved by our board of directors and stockholders in a prescribed manner or the interested stockholder acquired at least 85% of our outstanding voting stock in the transaction in which it became an interested stockholder. A "business combination" includes, among other things, a merger or consolidation involving us and the "interested stockholder" and the sale of more than 10% of our assets. In general, an "interested stockholder" is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person. The restrictions contained in Section 203 are not applicable to any of our existing stockholders that will own 15% or more of our outstanding voting stock upon the closing of this offering.

Staggered Board; Removal of Directors

Our certificate of incorporation and our bylaws to be effective upon the closing of this offering divide our board of directors into three classes with staggered three-year terms. In addition, our certificate of incorporation and our bylaws to be effective upon the closing of this offering provide that directors may be removed only for cause and only by the affirmative vote of the holders of 75% of our shares of capital stock present in person or by proxy and entitled to vote. Under our certificate of incorporation and our bylaws to be effective upon the closing of this offering, any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office. Furthermore, our certificate of incorporation to be effective upon the closing of this offering provides that the authorized number of directors may be changed only by the resolution of our board of directors. The classification of our board of directors and the limitations on the ability of our stockholders to remove directors, change the authorized number of directors and fill vacancies could make it more difficult for a third party to acquire, or discourage a third party from seeking to acquire, control of our company.

Stockholder Action; Special Meeting of Stockholders; Advance Notice Requirements for Stockholder Proposals and Director Nominations

Our certificate of incorporation and our bylaws to be effective upon the closing of this offering provide that any action required or permitted to be taken by our stockholders at an annual meeting or special meeting of stockholders may only be taken if it is properly brought before such meeting and may not be taken by written action in lieu of a meeting. Our certificate of incorporation and our bylaws to be effective upon the closing of this offering also provide that, except as otherwise required by law, special meetings of the stockholders can only be called by our board of directors. In addition, our bylaws to be effective upon the closing of this offering establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of stockholders, including proposed nominations of candidates for election to our board of directors. Stockholders at an annual meeting may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of our board of directors, or by a stockholder of record on the record date for the meeting who is entitled to vote

at the meeting and who has delivered timely written notice in proper form to our secretary of the stockholder's intention to bring such business before the meeting. These provisions could have the effect of delaying until the next stockholder meeting stockholder actions that are favored by the holders of a majority of our outstanding voting securities. These provisions also could discourage a third party from making a tender offer for our common stock because even if the third party acquired a majority of our outstanding voting stock, it would be able to take action as a stockholder, such as electing new directors or approving a merger, only at a duly called stockholders meeting and not by written consent.

Super-Majority Voting

The DGCL provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or bylaws unless a corporation's certificate of incorporation or bylaws, as the case may be, requires a greater percentage. Our bylaws to be effective upon the closing of this offering may be amended or repealed by a majority vote of our board of directors or the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in any annual election of directors. In addition, the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in any election of directors is required to amend or repeal or to adopt any provisions inconsistent with any of the provisions of our certificate of incorporation described above.

Exclusive Forum Selection

Our certificate of incorporation to be effective upon the closing of this offering provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if the Court of Chancery of the State of Delaware does not have jurisdiction, the federal district court for the District of Delaware) shall be the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, other employees or stockholders to our company or our stockholders, (3) any action asserting a claim arising pursuant to any provision of the DGCL or as to which the DGCL confers jurisdiction on the Court of Chancery of the State of Delaware or (4) any action asserting a claim arising pursuant to any provision of our certificate of incorporation or bylaws (in each case, as they may be amended from time to time) or governed by the internal affairs doctrine. This exclusive forum provision will not apply to actions arising under the Securities Act or the Exchange Act. Although our certificate of incorporation contains the choice of forum provision described above, it is possible that a court could rule that such a provision is inapplicable for a particular claim or action or that such provision is unenforceable.

Registration Rights

We have entered into an amended and restated investor rights agreement dated as of August 24, 2018, or the investor rights agreement, with holders of our preferred stock. Beginning six months following the closing of this offering, holders of a total of 114,500,000 shares of our common stock will have the right to require us to register these shares under the Securities Act under specified circumstances. We refer to the shares with these registration rights as registrable securities. After registration pursuant to these rights, the registrable securities will become freely tradable without restriction under the Securities Act.

Demand and Form S-3 Registration Rights

Beginning 180 days after this offering, subject to specified limitations set forth in the investor rights agreement, at any time, the holders of at least 40% of the then outstanding registrable securities may demand that we register at least 40% of the registrable securities then outstanding under the Securities Act for purposes of a public offering having an aggregate offering price to the public of not less than

\$5.0 million. We are not obligated to file a registration statement pursuant to this provision on more than two occasions.

In addition, subject to specified limitations set forth in the investor rights agreement, at any time after we become eligible to file a registration statement on Form S-3, the holders of at least 25% of the then outstanding registrable securities may request that we register their registrable securities on Form S-3 for purposes of a public offering for which the reasonably anticipated aggregate offering price to the public would be at least \$3.0 million. We are not obligated to file a registration statement pursuant to this provision on more than two occasions in any 12-month period.

Incidental Registration Rights

If, at any time after the closing of this offering, we propose to register for our own account any of our securities under the Securities Act, the holders of registrable securities will be entitled to notice of the registration and, subject to specified exceptions, have the right to require us to use our commercially reasonable efforts to register all or a portion of the registrable securities then held by them in that registration.

In the event that any registration in which the holders of registrable securities participate pursuant to our investor rights agreement is an underwritten public offering, we have agreed to enter into an underwriting agreement in usual and customary form and use our reasonable best efforts to facilitate such offering.

Expenses

Pursuant to the investor rights agreement, we are required to pay all registration expenses, including all registration and filing fees, exchange listing fees, printing expenses, fees and expenses of one counsel selected by the selling stockholders to represent the selling stockholders, state Blue Sky fees and expenses, and the expense of any special audits incident to or required by any such registration, but excluding underwriting discounts, selling commissions, stock transfer taxes applicable to the sale any registrable securities and the fees and expenses of the selling stockholders' own counsel (other than the counsel selected to represent all selling stockholders). If a registration is withdrawn at the request of the stockholders initiating the registration, then the stockholders will bear the expenses of the registration.

The investor rights agreement contains customary cross-indemnification provisions, pursuant to which we are obligated to indemnify the selling stockholders in the event of material misstatements or omissions in the registration statement attributable to us or any violation or alleged violation whether by action or inaction by us under the Securities Act, the Exchange Act, any state securities or Blue Sky law or any rule or regulation promulgated under the Securities Act, the Exchange Act or any state securities or Blue Sky law in connection with such registration statement or the qualification or compliance of the offering, and they are obligated to indemnify us for material misstatements or omissions in the registration statement attributable to them.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock will be Computershare Trust Company N.A.

Nasdaq Global Market

We have applied to have our common stock listed on the Nasdaq Global Market under the symbol "FULC."

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our common stock, and a liquid trading market for our common stock may not develop or be sustained after this offering. Future sales of substantial amounts of our common stock in the public market, including shares issued upon exercise of outstanding options, or the anticipation of these sales, could adversely affect market prices prevailing from time to time and could impair our ability to raise capital through sales of equity securities.

Upon the closing of this offering, we will have outstanding _____ shares of our common stock, based on the 19,430,506 shares of our common stock that were outstanding on April 30, 2019, after giving effect to the issuance of _____ shares of our common stock in this offering, assuming no exercise by the underwriters of their option to purchase additional shares of our common stock, and the conversion of all outstanding shares of our preferred stock into an aggregate of 112,500,000 shares of our common stock upon the closing of this offering. Of these shares, all shares sold in this offering will be freely tradable without restriction under the Securities Act of 1933, as amended, or the Securities Act, unless purchased by our "affiliates," as that term is defined in Rule 144 under the Securities Act. The remaining _____ shares of our common stock will be "restricted securities" under Rule 144, and we expect that substantially all of these restricted securities will be subject to the 180-day lock-up period under the lock-up agreements as described below. These restricted securities may be sold in the public market upon release or waiver of any applicable lock-up agreements and only if registered or pursuant to an exemption from registration, such as Rule 144 or Rule 701 under the Securities Act.

Rule 144

In general, under Rule 144, beginning 90 days after the date of this prospectus, any person who is not our affiliate and has held their shares for at least six months, including the holding period of any prior owner other than one of our affiliates, may sell those shares without restriction, subject to the availability of current public information about us. In addition, under Rule 144, any person who is not our affiliate and has not been our affiliate at any time during the preceding three months and has held their shares for at least one year, including the holding period of any prior owner other than one of our affiliates, would be entitled to sell an unlimited number of shares immediately upon the closing of this offering without regard to whether current public information about us is available.

Beginning 90 days after the date of this prospectus, a person who is our affiliate or who was our affiliate at any time during the preceding three months and who has beneficially owned restricted securities for at least six months, including the holding period of any prior owner other than one of our affiliates, is entitled to sell a number of shares within any three-month period that does not exceed the greater of:

- 1% of the number of shares of our common stock then outstanding, which will equal approximately _____ shares immediately after this offering; and
- the average weekly trading volume in our common stock on the Nasdaq Global Market during the four calendar weeks preceding the date of filing of a Notice of Proposed Sale of Securities Pursuant to Rule 144 with respect to the sale.

Sales under Rule 144 by our affiliates are also subject to manner of sale provisions and notice requirements and to the availability of current public information about us.

Upon waiver or expiration of the 180-day lock-up period described below, approximately _____ shares of our common stock will be eligible for sale under Rule 144. We cannot estimate the number of shares of our common stock that our existing stockholders will elect to sell under Rule 144.

Rule 701

In general, under Rule 701 of the Securities Act, any of our employees, consultants or advisors, other than our affiliates, who purchased shares from us in connection with a qualified compensatory stock plan or other written agreement is eligible to resell these shares 90 days after the date of this prospectus in reliance on Rule 144, but without compliance with the various restrictions, including the availability of public information about us, holding period and volume limitations, contained in Rule 144. Subject to the 180-day lock-up period described below, approximately _____ shares of our common stock, based on shares outstanding as of _____, 2019 will be eligible for sale in accordance with Rule 701.

Lock-up Agreements

We, each of our executive officers and directors and the holders of a majority of our outstanding securities have agreed that, without the prior written consent of Morgan Stanley & Co. LLC, BofA Securities, Inc. and SVB Leerink LLC, on behalf of the underwriters, we and they will not, subject to limited exceptions, during the period ending 180 days after the date of this prospectus:

- offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of, directly or indirectly, any shares of common stock or any securities convertible into or exercisable or exchangeable for shares of common stock, or make any public announcement of an intention to do any of the foregoing;
- file, or demand filing of, any registration statement with the SEC relating to the offering of any shares of common stock or any securities convertible into or exercisable or exchangeable for common stock; or
- enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the common stock, whether any such transaction is to be settled by delivery of common stock or such other securities, in cash or otherwise.

These agreements are subject to certain exceptions, as described in the section of this prospectus entitled "Underwriters."

Registration Rights

Beginning six months after the closing of this offering, the holders of an aggregate of 114,500,000 shares of our common stock will have rights, subject to certain conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. After registration pursuant to these rights, these shares will become freely tradable without restriction under the Securities Act. See "Description of Capital Stock—Registration Rights" for additional information regarding these registration rights.

Stock Options and Form S-8 Registration Statement

As of April 30, 2019, we had outstanding options to purchase an aggregate of 10,503,582 shares of our common stock under the 2016 Plan, of which options to purchase 354,098 shares were vested. Following this offering, we intend to file a registration statement on Form S-8 under the Securities Act to register all of the shares of our common stock subject to outstanding options and reserved for future options and other awards under the 2016 Plan, the 2019 Plan and the 2019 ESPP. See "Executive Compensation—Stock Option and Other Compensation Plans" for additional information regarding these plans. Accordingly, shares of our common stock registered under the registration statements will be available for sale in the open market, subject to Rule 144 volume limitations applicable to affiliates, and subject to any vesting restrictions and lock-up agreements applicable to these shares.

**MATERIAL U.S. FEDERAL INCOME AND ESTATE TAX CONSIDERATIONS
FOR NON-U.S. HOLDERS OF COMMON STOCK**

The following is a discussion of material U.S. federal income and estate tax considerations relating to the ownership and disposition of shares of our common stock acquired in this offering by a non-U.S. holder. For purposes of this discussion, the term "non-U.S. holder" means a beneficial owner (other than a partnership or other pass-through entity) of our common stock that is not, for U.S. federal income tax purposes:

- an individual who is a citizen or resident of the United States;
- a corporation, or other entity treated as a corporation, created or organized in or under the laws of the United States, any state thereof or the District of Columbia;
- an estate the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust if (1) a U.S. court is able to exercise primary supervision over the administration of the trust and one or more U.S. persons have authority to control all substantial decisions of the trust or (2) the trust has a valid election in effect under applicable U.S. Treasury Regulations to be treated as a U.S. person.

This discussion does not address the tax treatment of partnerships or other entities that are pass-through entities for U.S. federal income tax purposes or persons who hold shares of our common stock through partnerships or such other pass-through entities. The tax treatment of a partner in a partnership or other entity that is treated as a pass-through entity for U.S. federal income tax purposes generally will depend upon the status of the partner and the activities of the partnership. A partner in a partnership or other pass-through entity that will hold our common stock should consult his, her or its own tax advisor regarding the tax consequences of the ownership and disposition of our common stock through a partnership or other pass-through entity, as applicable.

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, which we refer to as the Code, existing and proposed U.S. Treasury Regulations promulgated thereunder, current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus and all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any change or differing interpretation could alter the tax consequences to non-U.S. holders described in this prospectus. There can be no assurance that the Internal Revenue Service, or the IRS, will not challenge one or more of the tax consequences described in this prospectus.

This discussion addresses only non-U.S. holders that hold shares of our common stock as a capital asset (generally, property held for investment) for U.S. federal income tax purposes. This discussion does not address all aspects of U.S. federal income and estate taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder's individual circumstances nor does it address any aspects of U.S. state, local or non-U.S. taxes, the alternative minimum tax, or the Medicare tax on net investment income. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as:

- financial institutions;
- brokers or dealers in securities;
- tax-exempt or governmental organizations;
- pension plans;
- owners that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment or who have elected to mark securities to market;

- insurance companies;
- controlled foreign corporations;
- passive foreign investment companies;
- non-U.S. governments; and
- certain U.S. expatriates.

THIS DISCUSSION IS FOR INFORMATION ONLY AND IS NOT, AND IS NOT INTENDED TO BE, LEGAL OR TAX ADVICE. PROSPECTIVE INVESTORS SHOULD CONSULT THEIR OWN TAX ADVISORS REGARDING THE U.S. FEDERAL, STATE, LOCAL, ESTATE AND NON-U.S. INCOME AND OTHER TAX CONSIDERATIONS OF ACQUIRING, HOLDING AND DISPOSING OF OUR COMMON STOCK, INCLUDING THE CONSEQUENCES OF ANY PROPOSED CHANGES IN APPLICABLE LAWS.

Distributions

As discussed under the heading "Dividend Policy" above, we do not expect to pay cash dividends to holders of our common stock in the foreseeable future. If we make distributions in respect of our common stock, those distributions generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder's investment, up to the non-U.S. holder's tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below under the heading "Gain on Sale, Exchange or Other Taxable Disposition of Our Common Stock."

Subject to the discussions below under the headings "Information Reporting and Backup Withholding" and "FATCA", dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence. A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder's country of residence generally will be required to provide a properly executed IRS Form W-8BEN or W-8BEN-E (or successor form) and satisfy applicable certification and other requirements. A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim with the IRS. Non-U.S. holders are urged to consult their own tax advisors regarding their entitlement to benefits under a relevant income tax treaty and the specific methods available to them to satisfy these requirements.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States, and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements (generally including provision of a properly executed IRS Form W-8ECI (or applicable successor form) certifying that the dividends are effectively connected with the non-U.S. holder's conduct of a trade or business within the United States). However, such U.S. effectively connected income is taxed on a net income basis at the same U.S. federal income tax rates applicable to U.S. persons (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is classified as a corporation for U.S. federal income tax purposes may also, under certain circumstances, be subject to an additional "branch profits tax" at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence.

Gain on Sale, Exchange or Other Taxable Disposition of Our Common Stock

A non-U.S. holder generally will not be subject to U.S. federal income tax on gain recognized on the non-U.S. holder's sale, exchange or other disposition of our common stock unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a trade or business in the United States, and, if an applicable income tax treaty so provides, the gain is attributable to a permanent establishment or fixed base maintained by the non-U.S. holder in the United States, in which case, the non-U.S. holder generally will be taxed on a net income basis at the U.S. federal income tax rates applicable to U.S. persons (as defined in the Code) and, if the non-U.S. holder is a foreign corporation, an additional branch profits tax at a rate of 30% (or a lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence) may also apply;
- the non-U.S. holder is a non-resident alien present in the United States for 183 days or more in the taxable year of the disposition and certain other requirements are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence) on the net gain derived from the disposition, which may be offset by certain U.S.-source capital losses of the non-U.S. holder, if any; or
- we are, or have been, at any time during the five-year period preceding such disposition (or the non-U.S. holder's holding period, if shorter) a "U.S. real property holding corporation," unless our common stock is regularly traded on an established securities market and the non-U.S. holder held no more than 5% of our outstanding common stock, directly or indirectly, during the shorter of the five-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. If we are determined to be a "U.S. real property holding corporation" and the foregoing exception does not apply, then the non-U.S. holder generally will be taxed on its net gain derived from the disposition at the U.S. federal income tax rates applicable to U.S. persons (as defined in the Code). Generally, a corporation is a "U.S. real property holding corporation" only if the fair market value of its "U.S. real property interests" (as defined in the Code and applicable regulations) equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we do not believe that we are, or have been, a "U.S. real property holding corporation" for U.S. federal income tax purposes, or that we are likely to become one in the future. No assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rule described above.

U.S. Federal Estate Tax

Shares of our common stock that are owned or treated as owned by an individual who is not a citizen or resident of the United States (as specially defined for U.S. federal estate tax purposes) at the time of such individual's death are considered U.S.-situs assets and will be included in the individual's gross estate for U.S. federal estate tax purposes. Such shares, therefore, may be subject to U.S. federal estate tax, unless an applicable estate tax or other treaty provides otherwise.

Information Reporting and Backup Withholding

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock paid to such holder and the tax withheld, if any, with respect to such distributions. Non-U.S. holders generally will have to comply with specific certification procedures to establish that the holder is not a U.S. person (as defined in the Code) in order to avoid backup withholding at the applicable rate with respect to dividends on our common stock. Generally, a non-U.S. holder will comply with such procedures if it provides a properly executed IRS Form W-8BEN or W-8BEN-E (or other applicable IRS

Form W-8), or otherwise meets documentary evidence requirements for establishing that it is a non-U.S. holder, or otherwise establishes an exemption. Dividends paid to non-U.S. holders subject to withholding of U.S. federal income tax, as described above under the heading "—Distributions," will generally be exempt from U.S. backup withholding.

Information reporting and backup withholding generally will apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or non-U.S., unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Non-U.S. holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement.

Backup withholding is not an additional tax. Rather, any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that an appropriate claim is timely filed with the IRS.

FATCA

Provisions of the Code commonly referred to as the Foreign Account Tax Compliance Act, or FATCA, generally impose a 30% withholding tax on dividends on, and, subject to the discussion below with respect to proposed U.S. Treasury Regulations excluding gross proceeds from such required withholding, gross proceeds from the sale or other disposition of, our common stock if paid to a foreign entity unless (i) if the foreign entity is a "foreign financial institution," the foreign entity undertakes certain due diligence, reporting, withholding and certification obligations, (ii) if the foreign entity is not a "foreign financial institution," the foreign entity identifies certain of its U.S. investors, if any, or (iii) the foreign entity is otherwise excepted under FATCA.

Withholding under FATCA generally applies to payments of dividends on our common stock. While withholding under FATCA may apply to payments of gross proceeds from a sale or other disposition of our common stock, under recently proposed U.S. Treasury Regulations withholding on payments of gross proceeds is not required. Although such regulations are not final, applicable withholding agents may rely on the proposed regulations until final regulations are issued.

If withholding under FATCA is required on any payment related to our common stock, investors not otherwise subject to withholding (or that otherwise would be entitled to a reduced rate of withholding) on such payment may be required to seek a refund or credit from the IRS. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this section. Non-U.S. holders should consult their own tax advisors regarding the possible implications of FATCA on their investment in our common stock and the entities through which they hold our common stock, including, without limitation, the process and deadlines for meeting the applicable requirements to prevent the imposition of the 30% withholding tax under FATCA.

The preceding discussion of material U.S. federal tax considerations is for information only. It is not, and is not intended to be, legal or tax advice. Prospective investors should consult their own tax advisors regarding the particular U.S. federal, state, local, estate and non-U.S. income and other tax consequences of acquiring, holding and disposing of our common stock, including the consequences of any proposed changes in applicable laws.

UNDERWRITERS

Under the terms and subject to the conditions in an underwriting agreement to be dated the date of this prospectus, the underwriters named below will severally agreed to purchase, and we will agree to sell to them, severally, the number of shares indicated below:

<u>Name</u>	<u>Number of Shares</u>
Morgan Stanley & Co. LLC	
BofA Securities, Inc.	
SVB Leerink LLC	
Total:	

The underwriters are collectively referred to as the "underwriters". The underwriters will offer the shares of common stock subject to their acceptance of the shares from us and subject to prior sale. The underwriting agreement will provide that the obligations of the several underwriters to pay for and accept delivery of the shares of common stock offered by this prospectus are subject to the approval of certain legal matters by their counsel and to certain other conditions. The underwriters will be obligated to take and pay for all of the shares of common stock offered by this prospectus if any such shares are taken. However, the underwriters will not be required to take or pay for the shares covered by the underwriters' over-allotment option described below.

The underwriters initially propose to offer part of the shares of common stock directly to the public at the offering price listed on the cover page of this prospectus and part to certain dealers at a price that represents a concession not in excess of \$ _____ per share under the public offering price. After the initial offering of the shares of common stock, the offering price and other selling terms may from time to time be varied by the underwriters.

We will grant to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase up to _____ additional shares of common stock at the public offering price listed on the cover page of this prospectus, less underwriting discounts and commissions. The underwriters may exercise this option solely for the purpose of covering over-allotments, if any, made in connection with the offering of the shares of common stock offered by this prospectus. To the extent the option is exercised, each underwriter will become obligated, subject to certain conditions, to purchase about the same percentage of the additional shares of common stock as the number listed next to the underwriter's name in the preceding table bears to the total number of shares of common stock listed next to the names of all underwriters in the preceding table.

The following table shows the per share and total public offering price, underwriting discounts and commissions, and proceeds before expenses to us. These amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase up to an additional _____ shares of common stock.

	<u>Per Share</u>	<u>Total</u>	
		<u>No Exercise</u>	<u>Full Exercise</u>
Public offering price	\$ _____	\$ _____	\$ _____
Underwriting discounts and commissions to be paid by us			
Proceeds, before expenses, to us	\$ _____	\$ _____	\$ _____

The estimated offering expenses payable by us, exclusive of the underwriting discounts and commissions, are approximately \$ _____. We have agreed to reimburse the underwriters for expenses relating to clearance of this offering with the Financial Industry Regulatory Authority up to \$ _____.

The underwriters have informed us that they do not intend sales to discretionary accounts to exceed 5% of the total number of shares of common stock offered by them.

We have applied to list our common stock on the Nasdaq Global Market under the symbol "FULC".

We and all of our directors and officers and the holders of all of our outstanding securities have agreed that, without the prior written consent of the underwriters, we and they will not, during the period ending 180 days after the date of this prospectus (the "restricted period"):

- offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of, directly or indirectly, any shares of common stock or any securities convertible into or exercisable or exchangeable for shares of common stock, or make any public announcement of an intention to do any of the foregoing;
- file, or demand filing of, any registration statement with the SEC relating to the offering of any shares of common stock or any securities convertible into or exercisable or exchangeable for common stock; or
- enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the common stock,

whether any such transaction described above is to be settled by delivery of common stock or such other securities, in cash or otherwise. In addition, we and each such person agrees that, without the prior written consent of the underwriters, we or such other person will not, during the restricted period, make any demand for, or exercise any right with respect to, the registration of any shares of common stock or any security convertible into or exercisable or exchangeable for common stock.

The restrictions on transfers or other dispositions by holders of our outstanding securities described in the immediately preceding paragraph do not apply to:

- transactions relating to shares of common stock or other securities acquired in this offering or in open market transactions after the completion of this offering, provided that no filing under Section 16(a) of the Exchange Act shall be required or shall be voluntarily made in connection with subsequent sales of common stock or other securities acquired in such open market transactions;
- transfers of shares of common stock or any security convertible into or exercisable or exchangeable for common stock as a bona fide gift or gifts, or to a charitable organization or educational institution in a transaction not involving a disposition for value;
- transfers of shares of common stock or any security convertible into or exercisable or exchangeable for common stock to any member of the immediate family of the signatory or any trust for the direct or indirect benefit of the signatory or the immediate family of the signatory in a transaction not involving a disposition for value;
- transfers of shares of common stock or any security convertible into or exercisable or exchangeable for common stock (i) by will, other testamentary document or intestate succession to the legal representative, heir, beneficiary or a member of the immediate family of the signatory upon the death of the signatory or (ii) solely by operation of law pursuant to a qualified domestic order or in connection with a divorce settlement;
- if the signatory is an entity, transfers or distributions of shares of common stock or any security convertible into common stock to general or limited partners, members or stockholders of the signatory, the signatory's direct and indirect affiliates, or to an investment fund or other entity that controls or manages, or is under common control with, the signatory;

- transfers or dispositions of shares of common stock or any security convertible into or exercisable or exchangeable for common stock to us pursuant to any contractual arrangement in effect on the date of the lock-up agreement and disclosed to the underwriters that provides for the repurchase of the signatory's common stock or other securities by us or in connection with the termination of the signatory's employment with or service to us; provided that, subject to certain limited exceptions, no filing under Section 16(a) of the Exchange Act reporting a reduction in beneficial ownership of shares of common stock shall be required or shall be voluntarily made during the restricted period in connection with any such transfers or dispositions;
- the conversion of outstanding shares of preferred stock described in this prospectus and outstanding as of the date of this prospectus into shares of common stock as described in this prospectus, provided that the shares of common stock received upon conversion shall be subject to the restrictions set forth in the lock-up agreement;
- the exercise of stock options to purchase shares of common stock granted under plans described in this prospectus and any related transfer to us of shares of common stock, subject to certain limitations, including that any shares of common stock received upon exercise shall be subject to the restrictions on transfer set forth in the lock-up agreement; provided that, subject to certain limited exceptions, no filing under Section 16(a) of the Exchange Act reporting a reduction in beneficial ownership of shares of common stock shall be required or shall be voluntarily made during the restricted period;
- the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of shares of common stock, provided that (i) such plan does not provide for the transfer of common stock during the restricted period and (ii) to the extent a public announcement or filing under the Exchange Act, if any, is required of or voluntarily made regarding the establishment of such plan, such announcement or filing shall include a statement to the effect that no transfer of common stock may be made under such plan during the restricted period; or
- (i) transfers of shares of common stock (or any securities convertible into or exercisable or exchangeable for common stock) pursuant to a bona fide third-party tender offer for shares of our capital stock made to all holders of securities, merger, consolidation or other similar transaction approved by our board of directors the result of which is a change of control or (ii) entry into any lock-up, voting or similar agreement pursuant to which the signatory may agree to transfer, sell, tender or otherwise dispose of shares of common stock or such other securities in connection with such a change of control;

provided that in the case of any transfer, disposition or distribution pursuant to the second, third, fourth or fifth bullet (i) each transferee, donee or distributee shall agree to be subject to the restrictions described in the immediately preceding paragraph and (ii) no filing under Section 16(a) of the Exchange Act, reporting a reduction in beneficial ownership of shares of common stock, shall be required or shall be voluntarily made during the restricted period (other than, in the case of a transfer or other disposition pursuant to the third bullet above, any Form 4 or Form 5 required to be filed under the Exchange Act if the signatory is subject to Section 16 reporting with respect to us under the Exchange Act and indicating by footnote disclosure or otherwise the nature of the transfer or disposition).

The restrictions on transfers or other dispositions by us described in the paragraph above do not apply to:

- the shares to be sold in this offering;
- the issuance by us of shares of common stock upon the exercise of an option or a warrant or the conversion of a security outstanding on the date of this prospectus pursuant to stock plans disclosed in this prospectus;

- the grant by us of any options to purchase shares of common stock or other awards granted under a stock incentive plan or stock purchase plan described in this prospectus, and the issuance by us of shares of common stock upon the exercise thereof, provided that we will cause each recipient of such grant to execute and deliver to the underwriters a lock-up agreement if such recipient has not already delivered one;
- the filing by the us of any registration statement on Form S-8 or a successor form thereto relating to the shares of common stock granted pursuant to or reserved for issuance under a stock incentive plan or stock purchase plan described in this prospectus; or
- shares of common stock or other securities issued in connection with a joint venture, equipment leasing arrangement, licensing or collaboration transaction or other strategic transaction with an unaffiliated third party, provided that (x) the aggregate number of shares issued pursuant to this exception will not exceed 5% of the total number of outstanding shares of common stock immediately following the issuance and sale of the shares to be sold in this offering and (y) the recipient of any such shares of common stock and securities issued pursuant to this exception during the restricted period will enter into a lock-up agreement.

The underwriters, in their sole discretion, may release the common stock and other securities subject to the lock-up agreements described above in whole or in part at any time.

In order to facilitate the offering of the common stock, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the common stock. Specifically, the underwriters may sell more shares than they are obligated to purchase under the underwriting agreement, creating a short position. A short sale is covered if the short position is no greater than the number of shares available for purchase by the underwriters under the over-allotment option. The underwriters can close out a covered short sale by exercising the over-allotment option or purchasing shares in the open market. In determining the source of shares to close out a covered short sale, the underwriters will consider, among other things, the open market price of shares compared to the price available under the over-allotment option. The underwriters may also sell shares in excess of the over-allotment option, creating a naked short position. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in this offering. As an additional means of facilitating this offering, the underwriters may bid for, and purchase, shares of common stock in the open market to stabilize the price of the common stock. These activities may raise or maintain the market price of the common stock above independent market levels or prevent or retard a decline in the market price of the common stock. The underwriters are not required to engage in these activities and may end any of these activities at any time.

We and the underwriters will agree to indemnify each other against certain liabilities, including liabilities under the Securities Act.

A prospectus in electronic format may be made available on websites maintained by one or more underwriters, or selling group members, if any, participating in this offering. The underwriters may agree to allocate a number of shares of common stock for sale to their online brokerage account holders. Internet distributions will be allocated to underwriters that may make Internet distributions on the same basis as other allocations.

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. Certain of the underwriters and their respective affiliates have, from time to time, performed,

and may in the future perform, various financial advisory and investment banking services for us, for which they received or will receive customary fees and expenses.

In addition, in the ordinary course of their various business activities, the underwriters and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers and may at any time hold long and short positions in such securities and instruments. Such investment and securities activities may involve our securities and instruments. The underwriters and their respective affiliates may also make investment recommendations or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long or short positions in such securities and instruments.

Pricing of the Offering

Prior to this offering, there has been no public market for our common stock. The initial public offering price will be determined by negotiations between us and the underwriters. Among the factors to be considered in determining the initial public offering price are our future prospects and those of our industry in general, our sales, earnings and certain other financial and operating information in recent periods, and the price-earnings ratios, price-sales ratios, market prices of securities, and certain financial and operating information of companies engaged in activities similar to ours.

Selling Restrictions

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a "Relevant Member State") an offer to the public of any shares of our common stock may not be made in that Relevant Member State, except that an offer to the public in that Relevant Member State of any shares of our common stock may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

- (a) to any legal entity which is a qualified investor as defined in the Prospectus Directive;
- (b) to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the underwriters for any such offer; or
- (c) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of shares of our common stock shall result in a requirement for the publication by us or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer to the public" in relation to any shares of our common stock in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and any shares of our common stock to be offered so as to enable an investor to decide to purchase any shares of our common stock, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State, the expression "Prospectus Directive" means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in the Relevant Member State, and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

United Kingdom

Each underwriter has represented and agreed that:

- (a) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000 ("FSMA") received by it in connection with the issue or sale of the shares of our common stock in circumstances in which Section 21(1) of the FSMA does not apply to us; and
- (b) it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the shares of our common stock in, from or otherwise involving the United Kingdom.

Japan

No registration pursuant to Article 4, paragraph 1 of the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948, as amended) (the "FIEL") has been made or will be made with respect to the solicitation of the application for the acquisition of the shares of common stock.

Accordingly, the shares of common stock have not been, directly or indirectly, offered or sold and will not be, directly or indirectly, offered or sold in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan) or to others for re-offering or re-sale, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan except pursuant to an exemption from the registration requirements, and otherwise in compliance with, the FIEL and the other applicable laws and regulations of Japan.

For Qualified Institutional Investors ("QII")

Please note that the solicitation for newly-issued or secondary securities (each as described in Paragraph 2, Article 4 of the FIEL) in relation to the shares of common stock constitutes either a "QII only private placement" or a "QII only secondary distribution" (each as described in Paragraph 1, Article 23-13 of the FIEL). Disclosure regarding any such solicitation, as is otherwise prescribed in Paragraph 1, Article 4 of the FIEL, has not been made in relation to the shares of common stock. The shares of common stock may only be transferred to QIIs.

For Non-QII Investors

Please note that the solicitation for newly-issued or secondary securities (each as described in Paragraph 2, Article 4 of the FIEL) in relation to the shares of common stock constitutes either a "small number private placement" or a "small number private secondary distribution" (each as is described in Paragraph 4, Article 23-13 of the FIEL). Disclosure regarding any such solicitation, as is otherwise prescribed in Paragraph 1, Article 4 of the FIEL, has not been made in relation to the shares of common stock. The shares of common stock may only be transferred en bloc without subdivision to a single investor.

Canada

Shares of our common stock may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 *Prospectus Exemptions* or subsection 73.3(1) of the *Securities Act* (Ontario), and are permitted clients, as defined in National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*. Any resale of shares of our common stock must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 (or, in the case of securities issued or guaranteed by the government of a non-Canadian jurisdiction, section 3A.4) of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Israel

This prospectus does not constitute a prospectus under the Israeli Securities Law, 5728-1968, and has not been filed with or approved by the Israel Securities Authority. In Israel, this prospectus is being distributed only to, and is directed only at, investors listed in the first addendum, or the Addendum, to the Israeli Securities Law, consisting primarily of joint investment in trust funds, provident funds, insurance companies, banks, portfolio managers, investment advisors, members of the Tel Aviv Stock Exchange, underwriters purchasing for their own account, venture capital funds, and entities with shareholders' equity in excess of NIS 50 million, each as defined in the Addendum (as it may be amended from time to time, collectively referred to as institutional investors). Institutional investors may be required to submit written confirmation that they fall within the scope of the Addendum. In addition, we may distribute and direct this prospectus in Israel, at our sole discretion, to certain other exempt investors or to investors who do not qualify as institutional or exempt investors, provided that the number of such non-qualified investors in Israel shall be no greater than 35 in any 12-month period.

Switzerland

The shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This prospectus has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this prospectus nor any other offering or marketing material relating to the shares or this offering may be publicly distributed or otherwise made publicly available in Switzerland. Neither this prospectus nor any other offering or marketing material relating to this offering, us, or the shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this prospectus will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, or FINMA, and the offer of shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares.

Dubai International Financial Centre

This prospectus relates to an Exempt Offer in accordance with the Offered Securities Rules of the Dubai Financial Services Authority, or DFSA. This prospectus is intended for distribution only to persons of a type specified in the Offered Securities Rules of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus nor taken steps to verify the information set forth herein and has no responsibility for the prospectus. The shares to which this prospectus relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the shares offered

should conduct their own due diligence on the shares. If you do not understand the contents of this prospectus you should consult an authorized financial advisor.

United Arab Emirates

The shares have not been, and are not being, publicly offered, sold, promoted or advertised in the United Arab Emirates (including the Dubai International Financial Centre) other than in compliance with the laws of the United Arab Emirates (and the Dubai International Financial Centre) governing the issue, offering and sale of securities. Further, this prospectus does not constitute a public offer of securities in the United Arab Emirates (including the Dubai International Financial Centre) and is not intended to be a public offer. This prospectus has not been approved by or filed with the Central Bank of the United Arab Emirates, the Securities and Commodities Authority or the Dubai Financial Services Authority.

Australia

No placement document, prospectus, product disclosure statement or other disclosure document has been lodged with the Australian Securities and Investments Commission, or ASIC, in relation to this offering. This prospectus does not constitute a prospectus, product disclosure statement or other disclosure document under the Corporations Act 2001, or the Corporations Act, and does not purport to include the information required for a prospectus, product disclosure statement or other disclosure document under the Corporations Act.

Any offer in Australia of the shares may only be made to persons, or the Exempt Investors, who are "sophisticated investors" (within the meaning of section 708(8) of the Corporations Act), "professional investors" (within the meaning of section 708(11) of the Corporations Act) or otherwise pursuant to one or more exemptions contained in section 708 of the Corporations Act so that it is lawful to offer the shares without disclosure to investors under Chapter 6D of the Corporations Act.

The shares applied for by Exempt Investors in Australia must not be offered for sale in Australia in the period of 12 months after the date of allotment under this offering, except in circumstances where disclosure to investors under Chapter 6D of the Corporations Act would not be required pursuant to an exemption under section 708 of the Corporations Act or otherwise or where the offer is pursuant to a disclosure document which complies with Chapter 6D of the Corporations Act. Any person acquiring shares must observe such Australian on-sale restrictions.

This prospectus contains general information only and does not take into account the investment objectives, financial situation or particular needs of any particular person. It does not contain any securities recommendations or financial product advice. Before making an investment decision, investors need to consider whether the information in this prospectus is appropriate for their needs, objectives and circumstances, and, if necessary, seek expert advice on those matters.

Hong Kong

The shares have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or (b) in other circumstances which do not result in the document being a "prospectus" as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance. No advertisement, invitation or document relating to the shares has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to the shares which are or are intended to be disposed of only to persons outside Hong Kong or only to

"professional investors" as defined in the Securities and Futures Ordinance and any rules made under that Ordinance.

Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of our shares may not be circulated or distributed, nor may our shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (1) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, (2) to a relevant person or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275 of the SFA, or (3) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA, in each case subject to compliance with conditions set forth in the SFA.

Where our shares are subscribed or purchased under Section 275 by a relevant person which is: (a) a corporation (which is not an accredited investor as defined in Section 4A of the SFA) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor; shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares under Section 275 of the SFA, except: (1) to an institutional investor (for corporations under Section 274 of the SFA) or to a relevant person defined in Section 275(2) of the SFA, or to any person pursuant to an offer that is made on terms that such shares, debentures and units of shares and debentures of that corporation or such rights and interest in that trust are acquired at a consideration of not less than \$200,000 (or its equivalent in a foreign currency) for each transaction, whether such amount is to be paid for in cash or by exchange of securities or other assets, and further for corporations, in accordance with the conditions, specified in Section 275 of the SFA; (2) where no consideration is or will be given for the transfer; or (3) where the transfer is by operation of law.

Saudi Arabia

This prospectus may not be distributed in the Kingdom of Saudi Arabia except to such persons as are permitted under the Offers of Securities Regulations as issued by the board of the Saudi Arabian Capital Market Authority, or the CMA pursuant to resolution number 2-11-2004 dated 4 October 2004 as amended by resolution number 1-28-2008, as amended, or the CMA Regulations. The CMA does not make any representation as to the accuracy or completeness of this prospectus and expressly disclaims any liability whatsoever for any loss arising from, or incurred in reliance upon, any part of this prospectus. Prospective purchasers of the shares offered hereby should conduct their own due diligence on the accuracy of the information relating to the shares. If you do not understand the contents of this prospectus, you should consult an authorized financial adviser.

China

This prospectus does not constitute a public offer of shares, whether by sale or subscription, in the People's Republic of China, or the PRC. The shares are not being offered or sold directly or indirectly in the PRC to or for the benefit of, legal or natural persons of the PRC.

Further, no legal or natural persons of the PRC may directly or indirectly purchase any of the shares or any beneficial interest therein without obtaining all prior PRC's governmental approvals that are

required, whether statutorily or otherwise. Persons who come into possession of this prospectus are required by the issuer and its representatives to observe these restrictions.

Korea

The shares have not been and will not be registered under the Financial Investments Services and Capital Markets Act of Korea and the decrees and regulations thereunder (the "FSCMA"), and the shares have been and will be offered in Korea as a private placement under the FSCMA. None of the shares may be offered, sold or delivered directly or indirectly, or offered or sold to any person for re-offering or resale, directly or indirectly, in Korea or to any resident of Korea except pursuant to the applicable laws and regulations of Korea, including the FSCMA and the Foreign Exchange Transaction Law of Korea and the decrees and regulations thereunder, or the FETL. The shares have not been listed on any of securities exchanges in the world including, without limitation, the Korea Exchange in Korea. Furthermore, the purchaser of the shares shall comply with all applicable regulatory requirements (including, but not limited to, requirements under the FETL) in connection with the purchase of the shares. By the purchase of the shares, the relevant holder thereof will be deemed to represent and warrant that if it is in Korea or is a resident of Korea, it purchased the shares pursuant to the applicable laws and regulations of Korea.

Taiwan

The shares have not been and will not be registered with the Financial Supervisory Commission of Taiwan pursuant to relevant securities laws and regulations and may not be sold, issued or offered within Taiwan through a public offering or in circumstances which constitutes an offer within the meaning of the Securities and Exchange Act of Taiwan that requires a registration or approval of the Financial Supervisory Commission of Taiwan. No person or entity in Taiwan has been authorized to offer, sell, give advice regarding or otherwise intermediate this offering and sale of the shares in Taiwan.

LEGAL MATTERS

The validity of the shares of common stock offered hereby is being passed upon for us by Wilmer Cutler Pickering Hale and Dorr LLP, Boston, Massachusetts. Ropes & Gray LLP, Boston, Massachusetts is acting as counsel for the underwriters in connection with this offering.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements at December 31, 2017 and 2018, and for each of the two years in the period ended December 31, 2018, as set forth in their report (which contains an explanatory paragraph describing conditions that raise substantial doubt about the company's ability to continue as a going concern as described in Note 1 to the consolidated financial statements). We have included our financial statements in the prospectus and elsewhere in the registration statement in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the shares of common stock we are offering to sell. This prospectus, which constitutes part of the registration statement, does not include all of the information contained in the registration statement and the exhibits, schedules and amendments to the registration statement. For further information with respect to us and our common stock, we refer you to the registration statement and to the exhibits and schedules to the registration statement. Statements contained in this prospectus about the contents of any contract, agreement or other document are not necessarily complete, and, in each instance, we refer you to the copy of the contract, agreement or other document filed as an exhibit to the registration statement. Each of these statements is qualified in all respects by this reference to such contract, agreement or document.

The SEC maintains an Internet website, which is located at <http://www.sec.gov>, that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC. You may access the registration statement of which this prospectus is a part at the SEC's Internet website. Upon completion of this offering, we will be subject to the information reporting requirements of the Securities Exchange Act of 1934, as amended, and we will file reports, proxy statements and other information with the SEC. We plan to fulfill our obligations with respect to such requirements by filing periodic reports and other information with the SEC. We intend to furnish our stockholders with annual reports containing financial statements certified by an independent registered public accounting firm. Our website address is www.fulcrumtx.com. The information contained on, or that can be accessed through, our website is not a part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

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Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Fulcrum Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Fulcrum Therapeutics, Inc. (the Company) as of December 31, 2018 and 2017, the related consolidated statements of operations and comprehensive loss, convertible preferred stock and stockholders' (deficit) equity and cash flows for the years then ended, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2018 and 2017, and the results of its operations and its cash flows for the years then ended, in conformity with U.S. generally accepted accounting principles.

The Company's Ability to Continue as a Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the consolidated financial statements, the Company has a history of losses and negative operating cash flows, will require additional capital to fund its current operating plan and has stated that substantial doubt exists about the Company's ability to continue as a going concern. Management's evaluation of the events and conditions and management's plans regarding these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2017.

Boston, Massachusetts

May 1, 2019

Fulcrum Therapeutics, Inc.

Consolidated Balance Sheets

(In thousands, except share and per share amounts)

	December 31, 2017	December 31, 2018	Pro Forma December 31, 2018 (Unaudited)
Assets			
Current assets:			
Cash and cash equivalents	\$ 407	\$ 72,797	\$ 72,797
Prepaid expenses and other current assets	931	1,298	1,298
Total current assets	1,338	74,095	74,095
Property and equipment, net	2,942	10,546	10,546
Restricted cash	—	1,092	1,092
Other assets	60	38	38
Total assets	<u>\$ 4,340</u>	<u>\$ 85,771</u>	<u>\$ 85,771</u>
Liabilities, convertible preferred stock, and stockholders' (deficit) equity			
Current liabilities:			
Accounts payable	\$ 1,673	\$ 1,263	\$ 1,263
Accrued expenses and other current liabilities	1,112	2,497	2,497
Deferred lease incentive, current portion	—	469	469
Total current liabilities	2,785	4,229	4,229
Deferred rent, excluding current portion	199	1,402	1,402
Deferred lease incentive, excluding current portion	—	3,990	3,990
Other liabilities, excluding current portion	34	150	150
Total liabilities	3,018	9,771	9,771
Commitments and contingencies (Note 9)			
Series A convertible preferred stock, \$0.001 par value; 60,000,000 shares authorized as of December 31, 2017 and 2018; 34,666,666 and 60,000,000 shares issued and outstanding as of December 31, 2017 and 2018, respectively (liquidation preference of \$67,187 as of December 31, 2018); no shares issued or outstanding, pro forma as of December 31, 2018 (unaudited)			
	34,587	59,909	—
Series B convertible preferred stock, \$0.001 par value; no shares and 40,000,000 shares authorized as of December 31, 2017 and 2018, respectively; no shares and 40,000,000 shares issued and outstanding as of December 31, 2017 and 2018, respectively (liquidation preference of \$82,261 as of December 31, 2018); no shares issued or outstanding, pro forma as of December 31, 2018 (unaudited)			
	—	79,761	—
Stockholders' (deficit) equity:			
Common stock, \$0.001 par value; 80,000,000 and 135,000,000 shares authorized as of December 31, 2017 and 2018, respectively; 18,401,555 and 19,542,588 shares issued as of December 31, 2017 and 2018, respectively; 6,806,102 and 11,116,085 shares outstanding as of December 31, 2017 and 2018, respectively; 119,542,588 and 111,116,085 shares issued and outstanding, pro forma as of December 31, 2018 (unaudited)			
	7	11	111
Treasury stock, at cost; 56,250 and 469,169 shares as of December 31, 2017 and 2018, respectively; 469,169 shares, pro forma as of December 31, 2018 (unaudited)			
	—	—	—
Additional paid-in capital	2,264	4,443	144,013
Accumulated deficit	(35,536)	(68,124)	(68,124)
Total stockholders' (deficit) equity	(33,265)	(63,670)	76,000
Total liabilities, convertible preferred stock, and stockholders' (deficit) equity	<u>\$ 4,340</u>	<u>\$ 85,771</u>	<u>\$ 85,771</u>

The accompanying notes are an integral part of these financial statements.

Fulcrum Therapeutics, Inc.**Consolidated Statements of Operations and Comprehensive Loss****(In thousands, except per share data)**

	Year Ended	
	December 31,	
	2017	2018
Operating expenses:		
Research and development	\$ 18,494	\$ 25,184
General and administrative	4,499	8,314
Total operating expenses	22,993	33,498
Loss from operations	(22,993)	(33,498)
Other income, net:		
Interest income, net	1	518
Other income	28	392
Net loss and comprehensive loss	\$ (22,964)	\$ (32,588)
Cumulative convertible preferred stock dividends	(2,407)	(6,559)
Net loss attributable to common stockholders	\$ (25,371)	\$ (39,147)
Net loss per share attributable to common stockholders, basic and diluted	\$ (5.09)	\$ (4.45)
Weighted average number of common shares used in net loss per share attributable to common stockholders, basic and diluted	4,980	8,799
Pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited)		\$ (0.43)
Pro forma weighted average number of common shares used in net loss per share attributable to common stockholders, basic and diluted (unaudited)		76,655

The accompanying notes are an integral part of these financial statements.

Fulcrum Therapeutics, Inc.

Consolidated Statements of Convertible Preferred Stock and Stockholders' (Deficit) Equity

(In thousands, except share amounts)

	Series A Convertible Preferred Stock		Series B Convertible Preferred Stock		Common Stock		Treasury Stock		Additional Paid-In Capital	Accumulated Deficit	Total Stockholders' (Deficit) Equity
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount			
Balance at December 31, 2016	17,000,000	\$ 16,962	—	\$ —	3,559,520	\$ 4	—	\$ —	887	\$ (12,572)	\$ (11,681)
Issuance of Series A convertible preferred stock at \$1.00 per share, net of issuance costs of \$42	17,666,666	17,625	—	—	—	—	—	—	—	—	—
Issuance of common stock	—	—	—	—	3,246,582	3	—	—	6	—	9
Repurchase of unvested restricted stock awards	—	—	—	—	—	—	56,250	—	—	—	—
Stock-based compensation expense	—	—	—	—	—	—	—	—	1,371	—	1,371
Net loss	—	—	—	—	—	—	—	—	—	(22,964)	(22,964)
Balance at December 31, 2017	<u>34,666,666</u>	<u>\$ 34,587</u>	<u>—</u>	<u>\$ —</u>	<u>6,806,102</u>	<u>\$ 7</u>	<u>56,250</u>	<u>\$ —</u>	<u>2,264</u>	<u>\$ (35,536)</u>	<u>\$ (33,265)</u>
Issuance of Series A convertible preferred stock at \$1.00 per share, net of issuance costs of \$11	25,333,334	25,322	—	—	—	—	—	—	—	—	—
Issuance of Series B convertible preferred stock at \$2.00 per share, net of issuance costs of \$239	—	—	40,000,000	79,761	—	—	—	—	—	—	—
Issuance of common stock	—	—	—	—	4,309,983	4	—	—	20	—	24
Repurchase of unvested restricted stock awards	—	—	—	—	—	—	655,980	—	—	—	—
Retirement of treasury shares	—	—	—	—	—	—	(243,061)	—	—	—	—
Stock-based compensation expense	—	—	—	—	—	—	—	—	2,159	—	2,159
Net loss	—	—	—	—	—	—	—	—	—	(32,588)	(32,588)
Balance at December 31, 2018	<u>60,000,000</u>	<u>\$ 59,909</u>	<u>40,000,000</u>	<u>\$ 79,761</u>	<u>11,116,085</u>	<u>\$ 11</u>	<u>469,169</u>	<u>\$ —</u>	<u>4,443</u>	<u>\$ (68,124)</u>	<u>\$ (63,670)</u>
Pro forma convertible preferred stock and stockholders' equity (unaudited):											
Conversion of convertible preferred stock into common stock (unaudited)	(60,000,000)	(59,909)	(40,000,000)	(79,761)	100,000,000	100	—	—	139,570	—	139,670
Pro forma balance at December 31, 2018 (unaudited)	<u>—</u>	<u>\$ —</u>	<u>—</u>	<u>\$ —</u>	<u>111,116,085</u>	<u>\$ 111</u>	<u>469,169</u>	<u>\$ —</u>	<u>\$ 144,013</u>	<u>\$ (68,124)</u>	<u>\$ 76,000</u>

The accompanying notes are an integral part of these financial statements.

Fulcrum Therapeutics, Inc.
Consolidated Statements of Cash Flows
(In thousands)

	Year Ended December 31,	
	2017	2018
Operating activities		
Net loss	\$ (22,964)	\$ (32,588)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation expense	715	1,345
Stock-based compensation expense	1,371	2,159
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(334)	(40)
Other assets	61	22
Accounts payable	208	(20)
Accrued expenses and other current liabilities	713	1,223
Deferred rent and deferred lease incentive	156	5,337
Net cash used in operating activities	<u>(20,074)</u>	<u>(22,562)</u>
Investing activities		
Purchases of property and equipment	(1,908)	(8,981)
Net cash used in investing activities	<u>(1,908)</u>	<u>(8,981)</u>
Financing activities		
Proceeds from issuance of Series A convertible preferred stock, net of issuance costs	17,621	25,322
Proceeds from issuance of Series B convertible preferred stock, net of issuance costs	—	79,761
Principal payments on capital lease obligations	—	(70)
Proceeds from issuance of common stock	41	12
Net cash provided by financing activities	<u>17,662</u>	<u>105,025</u>
Net increase (decrease) in cash, cash equivalents and restricted cash	(4,320)	73,482
Cash, cash equivalents, and restricted cash, beginning of period	4,727	407
Cash, cash equivalents, and restricted cash, end of period	<u>\$ 407</u>	<u>\$ 73,889</u>
Supplemental cash flow information		
Cash paid for interest	\$ —	\$ 10
Non-cash investing and financing activities:		
Property and equipment purchases unpaid at end of period	\$ 390	\$ 174

The following table provides a reconciliation of the cash, cash equivalents, and restricted cash balances as of each of the periods shown above:

	December 31,	
	2017	2018
Cash and cash equivalents	\$ 407	\$ 72,797
Restricted cash	—	1,092
Total cash, cash equivalents, and restricted cash	<u>\$ 407</u>	<u>\$ 73,889</u>

The accompanying notes are an integral part of these financial statements.

Fulcrum Therapeutics, Inc.

Notes to Consolidated Financial Statements

1. Nature of the Business and Basis of Presentation

Fulcrum Therapeutics, Inc. (the "Company" or "Fulcrum") was incorporated in Delaware on August 18, 2015. The Company is focused on improving the lives of patients with genetically defined diseases in areas of high unmet medical need, with an initial focus on rare diseases.

The Company is subject to a number of risks similar to other companies in the biotechnology industry, including, but not limited to, risks of failure of preclinical studies and clinical trials, dependence on key personnel, protection of proprietary technology, reliance on third party organizations, risks of obtaining regulatory approval for any product candidate that it may develop, development by competitors of technological innovations, compliance with government regulations, and the need to obtain additional financing. Product candidates currently under development will require significant additional research and development efforts, including extensive preclinical and clinical testing and regulatory approval, prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel infrastructure and extensive compliance-reporting capabilities. Even if the Company's development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

Basis of Presentation

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Updates ("ASU") of the Financial Accounting Standards Board ("FASB").

Going Concern

The Company has incurred recurring losses and negative cash flows from operations since inception and has primarily funded its operations with proceeds from the issuance of convertible notes and convertible preferred stock. As of December 31, 2018, the Company had an accumulated deficit of \$68.1 million. The Company expects its operating losses and negative operating cash flows to continue into the foreseeable future as it continues to expand its research and development efforts. As of May 1, 2019, the issuance date of the consolidated financial statements for the year ended December 31, 2018, the Company expected that its cash and cash equivalents as of December 31, 2018 will be sufficient to fund its operating expenses and capital expenditure requirements into the first quarter of 2020. The future viability of the Company beyond that point is dependent on its ability to raise additional capital to finance its operations.

If the Company is unable to obtain additional funding, the Company could be forced to delay, reduce or eliminate some or all of its research and development programs, product portfolio expansion, or commercialization efforts, which could adversely affect its business prospects, or the Company may be unable to continue operations. The Company is seeking to complete an initial public offering ("IPO") of its common stock ("Common Stock"). In the event the Company does not complete an IPO, the Company expects to seek additional funding through private equity financings, debt financings, or other capital sources, including collaborations with other companies or other strategic transactions. Although management plans to pursue additional funding, there is no assurance that the Company will be successful in obtaining sufficient funding on terms acceptable to the Company to fund continuing operations, if at all.

Fulcrum Therapeutics, Inc.

Notes to Consolidated Financial Statements (Continued)

1. Nature of the Business and Basis of Presentation (Continued)

Based on its recurring losses and negative cash flows from operations since inception, expectation of continuing operating losses and negative cash flows from operations for the foreseeable future, and the need to raise additional capital to finance its future operations, management concluded that there is substantial doubt about the Company's ability to continue as a going concern within one year after the date that the consolidated financial statements for the year ended December 31, 2018 were issued.

The accompanying consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty. Accordingly, the consolidated financial statements have been prepared on a basis that assumes the Company will continue as a going concern and which contemplates the realization of assets and satisfaction of liabilities and commitments in the ordinary course of business.

2. Summary of Significant Accounting Policies

Principles of Consolidation

The accompanying consolidated financial statements include the accounts of the Company and its wholly owned subsidiary, Fulcrum Therapeutics Securities Corp., which is a Massachusetts subsidiary created to buy, sell, and hold securities. All intercompany transactions and balances have been eliminated.

Use of Estimates

The preparation of financial statements in accordance with GAAP requires management to make certain estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities as of the date of the financial statements, and the reported amount of expenses during the reported periods. Estimates inherent in the preparation of these consolidated financial statements include, but are not limited to, estimates related to accrued expenses, stock-based compensation expense, the fair value of the Common Stock and convertible preferred stock, and income taxes. The Company bases its estimates on historical experience and other market specific or other relevant assumptions it believes to be reasonable under the circumstances. On an ongoing basis, management evaluates its estimates as there are changes in circumstances, facts and experience. Actual results could differ from those estimates or assumptions.

Unaudited Pro Forma Financial Information

The accompanying unaudited pro forma balance sheet and statement of stockholders' (deficit) equity as of December 31, 2018 has been prepared to give effect, upon the closing of a qualified IPO, to the automatic conversion of all shares of convertible preferred stock outstanding as of December 31, 2018 into 100,000,000 shares of Common Stock. In the accompanying consolidated statements of operations and comprehensive loss, the unaudited pro forma basic and diluted net loss per share attributable to common stockholders for the year ended December 31, 2018 have been prepared to give effect, upon the closing of a qualified IPO, to the automatic conversion of all outstanding shares of convertible preferred stock as if the proposed IPO had occurred on the later of January 1, 2018 or the issuance date of the convertible preferred stock (see Note 12).

Cash and Cash Equivalents

Cash equivalents are highly liquid investments that are readily convertible into cash with original maturities of three months or less when purchased. These assets include investments in money market

Fulcrum Therapeutics, Inc.**Notes to Consolidated Financial Statements (Continued)****2. Summary of Significant Accounting Policies (Continued)**

funds that invest in U.S. Treasury obligations. The Company maintains its bank accounts at major financial institutions. The Company had no cash equivalents as of December 31, 2017.

Restricted Cash

Restricted cash represents the cash held to secure a letter of credit associated with the Company's facility lease.

Fair Value of Financial Instruments

The fair value of the Company's financial assets and liabilities reflects the Company's estimate of amounts that it would have received in connection with the sale of the assets or paid in connection with the transfer of the liabilities in an orderly transaction between market participants at the measurement date. In connection with measuring the fair value of its assets and liabilities, the Company seeks to maximize the use of observable inputs (market data obtained from sources independent from the Company) and to minimize the use of unobservable inputs (the Company's assumptions about how market participants would price assets and liabilities). The following fair value hierarchy is used to classify assets and liabilities based on the observable inputs and unobservable inputs used in order to value the assets and liabilities:

Level 1: Quoted prices in active markets for identical assets or liabilities. An active market for an asset or liability is a market in which transactions for the asset or liability occur with sufficient frequency and volume to provide pricing information on an ongoing basis.

Level 2: Observable inputs other than Level 1 inputs. Examples of Level 2 inputs include quoted prices in active markets for similar assets or liabilities and quoted prices for identical assets or liabilities in markets that are not active.

Level 3: Unobservable inputs based on the Company's assessment of the assumptions that market participants would use in pricing the asset or liability.

The Company's cash equivalents are carried at fair value, determined according to the fair value hierarchy described above (see Note 3).

Property and Equipment

Property and equipment are recorded at cost, net of accumulated depreciation. Maintenance and repairs to an asset that do not improve or extend its life are charged to operations. Depreciation expense is recorded using the straight-line method over the estimated useful life of the related asset as follows:

	<u>Estimated Useful Life (in years)</u>
Lab equipment	5
Furniture and fixtures	4
Computer equipment	3
Software	3
Leasehold improvements	Shorter of useful life or remaining lease term

Construction-in-progress is stated at cost, which includes direct costs attributable to the setup or construction of the related asset. Depreciation expense is not recorded on construction-in-progress until

Fulcrum Therapeutics, Inc.**Notes to Consolidated Financial Statements (Continued)****2. Summary of Significant Accounting Policies (Continued)**

the relevant assets are completed and put into use. When assets are retired or otherwise disposed of, the assets and related accumulated depreciation are eliminated from the accounts and any resulting gain or loss is reflected in the Company's consolidated statements of operations and comprehensive loss.

Impairment of Long-Lived Assets

Long-lived assets consist of property and equipment. The Company continually evaluates whether events or circumstances have occurred that indicate that the estimated remaining useful life of its long-lived assets may warrant revision or that the carrying value of these assets may be impaired. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use or disposition of an asset group are less than its carrying amount. The impairment loss would be based on the excess of the carrying value of the impaired asset group over its fair value, determined based on discounted cash flows. The Company did not record any impairment losses on long-lived assets during the years ended December 31, 2017 or 2018.

Deferred Issuance Costs

The Company capitalizes certain legal, professional, accounting and other third-party fees that are directly associated with in-process equity issuances as deferred issuance costs until such equity issuances are consummated. After consummation of the equity issuance, these costs are recorded as a reduction in the capitalized amount associated with the equity issuance. Should the planned financing be abandoned, the deferred issuance costs will be expensed immediately as a charge to operating expenses in the consolidated statement of operations and comprehensive loss. Deferred issuance costs as of December 31, 2018 were less than \$0.1 million. No deferred issuance costs were capitalized as of December 31, 2017.

Leases

Leases are classified at their inception as either operating or capital leases. The Company recognizes rent expense for its facility lease, which is classified as an operating lease, on a straight-line basis over the respective lease term, inclusive of rent escalation provisions and rent holidays. The difference between rent payments made and straight-line rent expense is recorded as deferred rent. Additionally, the Company recognizes tenant improvement allowances for its operating leases as a deferred lease incentive and amortizes the lease incentive as a reduction to rent expense on a straight-line basis over the respective lease term.

Research and Development Expenses

Research and development expenses include costs directly attributable to the conduct of research and development programs, including personnel-related expenses such as salaries, payroll taxes, benefits, and stock-based compensation expense, manufacturing and external costs related to outside vendors engaged to conduct both preclinical studies and clinical trials, laboratory supplies, depreciation on and maintenance of research equipment, and the allocable portions of facility costs, such as rent, utilities, repairs and maintenance, depreciation, and general support services. Expenditures relating to research and development are expensed in the period incurred. Nonrefundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

Fulcrum Therapeutics, Inc.**Notes to Consolidated Financial Statements (Continued)****2. Summary of Significant Accounting Policies (Continued)*****Research Contract Costs and Accruals***

The Company has entered into various research and development contracts with research institutions and other companies. The Company records accruals for estimated ongoing research costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the studies or trials, including invoices received and contracted costs. Significant judgments and estimates are made in determining the accrued balances at each reporting period. Actual results could differ from the Company's estimates.

Patent-Related Costs

Patent-related costs incurred in connection with patent applications are expensed as incurred due to the uncertainty about the recovery of the expenditure. Amounts incurred are classified as general and administrative expenses in the accompanying statements of operations.

Fair Value of Common Stock and Series B Convertible Preferred Stock

The Company determined the estimated fair value of Common Stock and Series B convertible preferred stock (the "Series B Preferred Stock") based on a number of objective and subjective factors, including, but not limited to, external market conditions affecting the biotechnology industry sector, the prices at which the Company sold shares of convertible preferred stock and the superior rights and preferences of securities senior to the Company's Common Stock at the time, and the likelihood and potential timing of achieving a liquidity event, such as an IPO, in light of prevailing market conditions. The Company utilized valuation methodologies in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, Valuation of Privately-Held-Company Equity Securities Issued as Compensation, to estimate the fair value of Common Stock and the Series B Preferred Stock. The methodologies utilized to estimate the fair value of Common Stock included the guideline public company method and/or the precedent transaction method to estimate the equity value, and the option-pricing method ("OPM") or the hybrid method, which is a probability-weighted expected return method ("PWERM"), to allocate equity value to the Common Stock and Preferred Stock. The Company utilized the hybrid method to estimate the fair value of the Series B Preferred Stock. Significant changes to the key assumptions used in the valuations could result in different fair values of Common Stock and the Series B Preferred Stock.

Stock-Based Compensation

The Company measures stock-based awards based on the fair value on the date of grant. Compensation expense of those awards is recognized over the requisite service period, which is generally the vesting period of the respective award. Generally, the Company issues awards with only service-based vesting conditions and records the expense for these awards using the straight-line method. The Company has also granted certain stock-based awards with performance-based vesting conditions. The Company records the expense for stock-based awards with performance-based vesting conditions over the remaining service period using an accelerated attribution method when management determines that achievement of the performance condition is probable. At each reporting date, the Company evaluates if the achievement of a performance-based milestone is probable based on the expected satisfaction of the performance conditions.

Fulcrum Therapeutics, Inc.**Notes to Consolidated Financial Statements (Continued)****2. Summary of Significant Accounting Policies (Continued)**

The fair value of each restricted stock award is based on the fair value of the Company's Common Stock on the grant date, less any applicable purchase price. The fair value of each stock option is estimated on the grant date using the Black-Scholes option-pricing model, which requires inputs based on certain subjective assumptions, including the fair value of the Company's Common Stock, the expected stock price volatility, the expected term of the award, the risk-free interest rate, and expected dividends. Expected volatility is calculated based on reported volatility data for a representative group of publicly traded companies for which historical information is available. The historical volatility is calculated based on a period of time commensurate with the assumption used for the expected term. The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the time of grant commensurate with the expected term assumption. The Company uses the simplified method, under which the expected term is presumed to be the midpoint between the vesting date and the end of the contractual term. The Company utilizes this method due to the lack of historical exercise data and the plain nature of its stock-based awards. The expected dividend yield is assumed to be zero as the Company has never paid dividends and has no current plans to pay any dividends on Common Stock.

The Company accounts for forfeitures as they occur (refer to the "Recently Adopted Accounting Pronouncements" below). The Company classifies stock-based compensation expense in its statements of operations in the same manner in which the award recipient's payroll or service costs are classified.

Income Taxes

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the consolidated financial statements or in the Company's tax returns. Under this method, deferred tax assets and liabilities are determined based on differences between the financial statement carrying amounts and the tax bases of the assets and liabilities using the enacted tax rates in effect in the years in which the differences are expected to reverse. A valuation allowance against deferred tax assets is recorded if, based on the weight of the available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. Potential for recovery of deferred tax assets is evaluated by considering several factors, including estimating the future taxable profits expected, estimating future reversals of existing taxable temporary differences, considering taxable profits in carryback periods, and considering prudent and feasible tax planning strategies.

The Company accounts for uncertain tax positions using a more-likely-than-not threshold for recognizing and resolving uncertain tax positions. The evaluation of uncertain tax positions is based on factors including, but not limited to, changes in the law, the measurement of tax positions taken or expected to be taken in tax returns, the effective settlement of matters subject to audit, new audit activity, and changes in facts or circumstances related to a tax position.

Comprehensive Loss

Comprehensive loss is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. For the years ended December 31, 2017 and 2018, comprehensive loss was equal to net loss.

Fulcrum Therapeutics, Inc.**Notes to Consolidated Financial Statements (Continued)****2. Summary of Significant Accounting Policies (Continued)*****Net Income (Loss) Per Share***

The Company applies the two-class method to compute basic and diluted net income (loss) per share attributable to common stockholders when it has issued shares that meet the definition of participating securities. The two-class method determines net income (loss) per share for each class of common and participating securities according to dividends declared or accumulated and participation rights in undistributed earnings. The two-class method requires income (loss) available to common stockholders for the period to be allocated between common and participating securities based upon their respective rights to share in the earnings as if all income (loss) for the period had been distributed. The Company's convertible preferred stock participates in any dividends declared by the Company and are therefore considered to be participating securities. The participating securities are not required to participate in the losses of the Company, and therefore during periods of loss there is no allocation required under the two-class method.

Basic net income (loss) per share attributable to common stockholders is computed by dividing the net income (loss) attributable to common stockholders by the weighted average number of shares of common stock outstanding for the period. Diluted net income (loss) attributable to common stockholders is computed by adjusting net income (loss) per share attributable to common stockholders to reallocate undistributed earnings based on the potential impact of dilutive securities. Diluted net income (loss) per share attributable to common stockholders is computed by dividing the diluted net income (loss) attributable to common stockholders by the weighted average number of shares of common stock outstanding for the period, including potential dilutive common shares. For purpose of this calculation, outstanding options to purchase Common Stock, unvested restricted stock awards, and shares of convertible preferred stock are considered potential dilutive common shares. The Company has generated a net loss in all periods presented, and therefore the basic and diluted net loss per share attributable to common stockholders are the same as the inclusion of the potentially dilutive securities would be anti-dilutive.

Off-Balance Sheet Risk and Concentrations of Credit Risk

The Company has no significant off-balance sheet risk such as foreign exchange contracts, option contracts, or other foreign hedging arrangements. Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash, cash equivalents, and restricted cash. The Company's cash, cash equivalents, and restricted cash are deposited in accounts at large financial institutions. The Company believes it is not exposed to significant credit risk due to the financial strength of the depository institutions in which the cash, cash equivalents and restricted cash are held. The Company maintains its cash equivalents in money market funds that invest in U.S. Treasury securities.

Segment Information

Operating segments are defined as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision-maker in making decisions regarding resource allocation and assessing performance. The Company and the Company's chief operating decision-maker, the Company's chief executive officer, view the Company's operations and manage its business as a single operating segment.

Fulcrum Therapeutics, Inc.**Notes to Consolidated Financial Statements (Continued)****2. Summary of Significant Accounting Policies (Continued)*****Emerging Growth Company Status***

The Company is an emerging growth company ("EGC"), as defined in the Jumpstart Our Business Startups Act (the "JOBS Act"), and may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not EGCs. The Company may take advantage of these exemptions until it is no longer an EGC under Section 107 of the JOBS Act, which provides that an EGC can take advantage of the extended transition period afforded by the JOBS Act for the implementation of new or revised accounting standards. The Company has elected to use the extended transition period for complying with new or revised accounting standards, and as a result of this election, its consolidated financial statements may not be comparable to companies that comply with public company effective dates for ASUs. The Company may take advantage of these exemptions up until the last day of the fiscal year following the fifth anniversary of an offering or such earlier time that it is no longer an EGC.

Recently Adopted Accounting Pronouncements

In May 2014, the FASB issued ASU No. 2014-09, *Revenue from Contracts with Customers (Topic 606)* ("ASU 2014-09"). The standard replaces existing revenue recognition standards and significantly expands the disclosure requirements for revenue arrangements. The standard must be adopted using either a modified retrospective approach or a full retrospective approach for all periods presented. The Company adopted the standard as of January 1, 2017 under the full retrospective method. The Company does not have and has never had any contracts that are within the scope of ASU 2014-09 or its predecessor guidance, ASC 605, *Revenue Recognition*. Accordingly, adoption of the standard did not have an impact on the Company's financial position, results of operations or cash flows. However, the adoption of this standard will impact the accounting for potential future revenue transactions.

In March 2016, the FASB issued ASU No. 2016-09, *Compensation—Stock Compensation* ("ASU 2016-09"), which amends ASC Topic 718, *Compensation—Stock Compensation* ("Topic 718"). The standard is intended to simplify various aspects of the accounting for share-based payments, including the income tax consequences, classification of awards as either equity or liabilities, an option to recognize gross share compensation expense with actual forfeitures recognized as they occur, as well as certain classifications on the statement of cash flows. The Company adopted ASU 2016-09 effective as of January 1, 2016. The Company elected to account prospectively for forfeitures as they occur rather than apply an estimated forfeiture rate to stock-based compensation expense. The adoption of the standard did not have a material impact on the Company's consolidated financial statements or footnote disclosures.

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments* ("ASU 2016-15"), which simplifies certain elements of cash flow classification. The standard is intended to reduce diversity in practice in how certain transactions are classified in the statement of cash flows. The Company adopted the standard effective as of January 1, 2016. The adoption of the standard did not have a material impact on the Company's consolidated financial statements or footnote disclosures.

In November 2016, the FASB issued ASU 2016-18, *Statement of Cash Flows (Topic 230): Restricted Cash* ("ASU 2016-18"). The standard requires that amounts generally described as restricted cash be included within cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on the statement of cash flows. The Company adopted ASU 2016-18 effective as of

Fulcrum Therapeutics, Inc.**Notes to Consolidated Financial Statements (Continued)****2. Summary of Significant Accounting Policies (Continued)**

January 1, 2016 using a full retrospective approach. The adoption of the standard did not have a material impact on the Company's consolidated financial statements or footnote disclosures.

In January 2017, the FASB issued ASU 2017-01, *Business Combinations (Topic 805): Clarifying the Definition of a Business* ("ASU 2017-01"). The standard clarifies the framework for determining whether an integrated set of assets and activities meets the definition of a business. The revised framework establishes a screen for determining whether an integrated set of assets and activities is a business and narrows the definition of a business. The screen requires that when substantially all of the fair value of the gross assets acquired (or disposed of) is concentrated in a single identifiable asset or a group of similar identifiable assets, the set is not a business. This screen reduces the number of transactions that need to be further evaluated. The Company adopted ASU 2017-01 effective as of January 1, 2018. The adoption of this standard did not have a material impact on the Company's consolidated financial statements or footnote disclosures.

In May 2017, the FASB issued ASU No. 2017-09, *Compensation—Stock Compensation (Topic 718): Scope of Modification Accounting* ("ASU 2017-09"). The standard is intended to reduce the diversity in practice and cost and complexity when applying the guidance in Topic 718 to a change to the terms or conditions of a share-based payment award. Under the guidance, modification accounting is required only if the fair value, the vesting conditions or the classification of the award (as equity or liability) changes as a result of the change in terms or conditions. The Company adopted ASU 2017-09 effective as of January 1, 2016. The adoption of this standard did not have a material impact on the Company's consolidated financial statements or footnote disclosures.

In June 2018, the FASB issued ASU No. 2018-07, *Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment* ("ASU 2018-07"). The standard is intended to simplify the accounting for share-based payments to non-employees by aligning it with the accounting for share-based payments to employees, with certain exceptions. Under the guidance, the measurement of equity-classified non-employee awards will be fixed at the grant date, which may lower their cost and reduce volatility in the income statement. The Company adopted ASU 2018-07 as of January 1, 2017. The adoption of this standard did not have a material impact on the Company's consolidated financial statements or footnote disclosures.

In August 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurement (Topic 820): Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurement* ("ASU 2018-13"). The standard eliminates, adds and modifies certain disclosure requirements for fair value measurements. The Company adopted ASU 2018-13 as of January 1, 2018. The adoption of this standard did not have a material impact on the Company's consolidated financial statements or footnote disclosures.

Recent Accounting Pronouncements—To Be Adopted

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)* ("ASU 2016-02"), as amended by various subsequently issued ASUs. The standard requires lessees to recognize an operating lease with a term greater than one year on their balance sheets as a right-of-use asset and corresponding lease liability, measured at the present value of the lease payments. Lessees are required to classify leases as either finance or operating leases. If the lease is effectively a financed-purchase by the lessee, it is classified as a financing lease, otherwise it is classified as an operating lease. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight-line basis over the term of the lease. In July 2018, the FASB also issued ASU 2018-11, *Leases (Topic 842)*:

Fulcrum Therapeutics, Inc.**Notes to Consolidated Financial Statements (Continued)****2. Summary of Significant Accounting Policies (Continued)**

Targeted Improvements ("ASU 2018-11"), which permits entities to continue applying legacy guidance in ASC 840, *Leases*, including its disclosure requirements, in the comparative periods presented in the year that the entity adopts the new leasing standard. The new standard will be effective for the Company on January 1, 2020 (refer to previous discussion under "Emerging Growth Company Status"). The Company will apply the transition method permitted by ASU 2018-11. The Company is currently evaluating the effect that adoption of the standard is expected to have on the Company's consolidated financial statements and related disclosures. The Company expects to take advantage of certain available expedients by electing the transition package of practical expedients permitted within ASU 2016-02, which allows the Company to not reassess previous accounting conclusions around whether arrangements are, or contain, leases, the classification of leases, and the treatment of initial direct costs. The Company also expects to make an accounting policy election to exclude leases with an initial term of twelve months or less from the balance sheet.

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments—Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* ("ASU 2016-13"). The standard requires that credit losses be reported using an expected losses model rather than the incurred losses model that is currently used, and establishes additional disclosures related to credit risks. For available-for-sale debt securities with unrealized losses, this standard requires allowances to be recorded instead of reducing the amortized cost of the investment. The new standard will be effective for the Company on January 1, 2021. The Company is currently evaluating the potential impact that this standard may have on its consolidated financial position and results of operations.

In July 2017, the FASB issued ASU No. 2017-11, *Earnings Per Share (Topic 260), Distinguishing Liabilities from Equity (Topic 480), Derivatives and Hedging (Topic 815) I. Accounting for Certain Financial Instruments with Down Round Features II. Replacement of the Indefinite Deferral for Mandatorily Redeemable Financial Instruments of Certain Nonpublic Entities and Certain Mandatorily Redeemable Noncontrolling Interests with a Scope Exception* ("ASU 2017-11"). Part I of the standard applies to entities that issue financial instruments such as warrants, convertible debt or convertible preferred stock that contain down-round features. Part II of the standard replaces the indefinite deferral for certain mandatorily redeemable noncontrolling interests and mandatorily redeemable financial instruments of nonpublic entities contained within ASC Topic 480 with a scope exception and does not impact the accounting for these mandatorily redeemable instruments. The new standard will be effective for the Company on January 1, 2020 (refer to previous discussion under "Emerging Growth Company Status"). The Company is currently evaluating the impact that the adoption of ASU 2017-11 will have on its consolidated financial statements.

3. Fair Value Measurements

The following table presents information about the Company's financial assets measured at fair value on a recurring basis and indicate the level of the fair value hierarchy utilized to determine such fair values as of December 31, 2018 (in thousands):

	<u>Total</u>	<u>Level 1</u>	<u>Level 2</u>	<u>Level 3</u>
Cash equivalents:				
Money market funds	\$ 72,797	\$ 72,797	\$ —	\$ —
Total	<u>\$ 72,797</u>	<u>\$ 72,797</u>	<u>\$ —</u>	<u>\$ —</u>

The Company had no cash equivalents as of December 31, 2017. There have been no transfers between fair value levels during the year ended December 31, 2018.

Fulcrum Therapeutics, Inc.**Notes to Consolidated Financial Statements (Continued)****4. Property and Equipment, Net**

Property and equipment, net consisted of the following (in thousands):

	December 31, 2017	December 31, 2018
Lab equipment	\$ 3,018	\$4,847
Furniture and fixtures	—	542
Computer equipment	281	517
Software	90	90
Leasehold improvements	280	6,174
Construction in process	166	334
Total property and equipment	3,835	12,504
Less: accumulated depreciation	(893)	(1,958)
Property and equipment, net	\$ 2,942	\$ 10,546

Depreciation expense for the years ended December 31, 2017 and 2018 was \$0.7 million and \$1.3 million, respectively. Total property and equipment, gross, as of December 31, 2017 and 2018 included zero and \$0.2 million, respectively, of property and equipment recorded under capital leases. Accumulated depreciation, as of December 31, 2017 and 2018, included zero and less than \$0.1 million, respectively, for property and equipment recorded under capital leases.

5. Additional Balance Sheet Detail

Prepaid expenses and other current assets consisted of the following (in thousands):

	December 31, 2017	December 31, 2018
Prepaid expenses	\$ 422	\$460
Prepaid sign-on bonuses subject to vesting provisions	222	99
Security deposits	90	—
Leasehold improvement allowance receivable	39	366
Interest income receivable	—	135
Other	158	238
Total prepaid expenses and other current assets	\$ 931	\$ 1,298

Fulcrum Therapeutics, Inc.**Notes to Consolidated Financial Statements (Continued)****5. Additional Balance Sheet Detail (Continued)**

Accrued expenses and other current liabilities consisted of the following (in thousands):

	December 31, 2017	December 31, 2018
External research and development	\$ 8	\$ 437
Payroll and benefits	1,004	1,448
Professional services	80	254
Capital lease obligation, current portion	—	46
Restricted stock liability, current portion	18	18
Property and equipment purchases	—	174
Other	2	120
Total accrued expenses and other current liabilities	<u>\$ 1,112</u>	<u>\$ 2,497</u>

Future minimum lease payments associated with the Company's capital lease obligations are less than \$0.1 million in each of the years ending December 31, 2019, 2020 and 2021. No minimum lease payments associated with the Company's capital lease obligations are due after December 31, 2021.

6. Convertible Preferred Stock

In July 2016, the Company entered into a Series A convertible preferred stock purchase agreement (the "2016 Stock Purchase Agreement"), which provided for the issuance and sale of up to 55,000,000 shares of Series A convertible preferred stock (the "Series A Preferred Stock") at a price of \$1.00 per share in three tranches, each of which could occur in multiple closings. Included in the terms of the Series A Preferred Stock purchase agreement were tranche rights. The tranche rights obligated the investors in the Series A Preferred Stock to purchase, and the Company to sell, shares of Series A Preferred Stock at \$1.00 per share, subject to the achievement of certain milestones related to the Company's research platform and organizational development. The specified milestones were waivable with the consent of the holders of a majority of the shares of Series A Preferred Stock.

During the year ended December 31, 2017, the Company sold 12,666,666 shares of Series A Preferred Stock under the 2016 Stock Purchase Agreement for aggregate proceeds of approximately \$12.7 million. During the year ended December 31, 2018, the Company sold the remaining 25,333,334 shares of Series A Preferred Stock under the 2016 Stock Purchase Agreement for aggregate proceeds of approximately \$25.3 million.

In April 2017, the Company increased the number of shares of Series A Preferred Stock authorized for issuance to 60,000,000 shares and entered into an additional Series A Preferred Stock purchase agreement (the "2017 Stock Purchase Agreement", and together with the 2016 Stock Purchase Agreement, the "Stock Purchase Agreements"), pursuant to which the Company sold 5,000,000 shares of Series A Preferred Stock for aggregate proceeds of \$5.0 million. The Company incurred issuance costs associated with the Stock Purchase Agreements of less than \$0.1 million during each of the years ended December 31, 2017 and 2018.

The Company determined that the tranche rights did not meet the definition of a freestanding financial instrument because, while separately exercisable, they were not legally detachable. Further, the Company determined that the embedded future tranche rights did not require bifurcation as they were

Fulcrum Therapeutics, Inc.

Notes to Consolidated Financial Statements (Continued)

6. Convertible Preferred Stock (Continued)

clearly and closely related to the economic characteristics and risks of the Series A Preferred Stock and did not meet the definition of a derivative on a standalone basis.

In August 2018, the Company entered into a Series B convertible preferred stock purchase agreement (the "Series B Stock Purchase Agreement"), pursuant to which the Company sold 40,000,000 shares of Series B Preferred Stock at a purchase price of \$2.00 per share for gross proceeds of \$80,000,000. In connection with the Series B Stock Purchase Agreement, the Company's Certificate of Incorporation was amended and restated to authorize the Company to issue 40,000,000 shares of Series B Preferred Stock. Refer to Note 14 for information regarding the issuance of Series B Preferred Stock subsequent to December 31, 2018.

The Company assessed the Series A Preferred Stock and the Series B Preferred Stock (together, the "Preferred Stock") for any beneficial conversion features or embedded derivatives, including the conversion option, that would require bifurcation from the Preferred Stock and receive separate accounting treatment. Based on the Company's determination that the Preferred Stock is an "equity host," the Company determined that all features of the Preferred Stock were either clearly and closely related to the equity host or did not meet the definition of a derivative, and therefore do not require bifurcation as a derivative liability. On the date of issuance, the estimated fair value of Common Stock into which the Preferred Stock was convertible was less than the effective conversion price of the Preferred Stock, and as such, there was no beneficial conversion feature at the commitment dates.

As the Preferred Stock may become redeemable upon the occurrence of a Deemed Liquidation Event (as defined below), the Preferred Stock has been classified outside of stockholders' deficit. Since the Preferred Stock is not initially redeemable and the Company has determined that it is not probable that it will become redeemable, the carrying value of the Preferred Stock has not been adjusted.

No dividends have been declared since inception. Aggregate cumulative dividends associated with the Series A Preferred Stock and the Series B Preferred Stock as of December 31, 2018 were \$7.2 million and \$2.3 million, respectively.

The holders of the Preferred Stock have the following rights, privileges, and preferences:

Voting Rights

The holders of the Preferred Stock are entitled to vote on all matters submitted to stockholders for a vote and have the right to vote the number of shares equal to the number of shares of Common Stock into which such shares of Preferred Stock could convert on the record date for determination of stockholders entitled to vote. The holders of Preferred Stock will vote together with the holders of Common Stock as a single class, on an as-converted basis, unless otherwise specified by law or the Certificate of Incorporation. For example, the holders of Series A Preferred Stock, exclusively and as a separate class, are entitled to elect one director of the Company and the holders of Series B Preferred Stock, exclusively and as a separate class, are entitled to elect one director of the Company.

Conversion

Each share of Preferred Stock is convertible, at the option of the holder, at any time, and without the payment of additional consideration by the holder, into such number of fully paid and nonassessable shares of Common Stock as is determined by dividing the Original Issue Price (as defined below) applicable to such series of Preferred Stock by the Conversion Price (as defined below) applicable to such series of

Fulcrum Therapeutics, Inc.**Notes to Consolidated Financial Statements (Continued)****6. Convertible Preferred Stock (Continued)**

Preferred Stock in effect at the time of conversion. The Original Issue Price is \$1.00 per share for Series A Preferred Stock and \$2.00 per share for Series B Preferred Stock, each subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Preferred Stock. The Conversion Price is initially \$1.00 per share for Series A Preferred Stock and \$2.00 per share for Series B Preferred Stock, each subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization and other adjustments, as set forth in the Company's Certificate of Incorporation, as amended and/or restated.

Each share of Preferred Stock will automatically convert into shares of Common Stock at the then-effective conversion ratio upon either (i) the closing of the sale of shares of Common Stock to the public in a firm-commitment underwritten public offering pursuant to an effective registration statement under the Securities Act of 1933, as amended (the "Securities Act"), provided that such offering results in at least \$45 million of gross proceeds to the Company and, following such offering, the Common Stock is listed on the New York Stock Exchange or Nasdaq or (ii) the date and time, or the occurrence of an event, specified by the vote or written consent of the holders of at least 65% of the outstanding shares of Preferred Stock. If the holders of at least 65% of the outstanding shares of Preferred Stock approve such a mandatory conversion in connection with a proposed Deemed Liquidation Event in which the holders of Series B Preferred Stock would receive less than the full liquidation preference applicable to the Series B Preferred Stock (as discussed below), then the mandatory conversion will also require the consent of the holders of a majority of the outstanding shares of Series B Preferred Stock, voting together as a separate class.

Dividends

From the date of issuance of the Series B Preferred Stock, dividends at an annual rate of \$0.16 per share will accrue on such shares of Series B Preferred Stock, subject to adjustment in the event of any stock split, stock dividend, or other similar recapitalization with respect to the Series B Preferred Stock (the "Series B Accruing Dividends"). From the date of issuance of the Series A Preferred Stock, dividends at an annual rate of \$0.08 per share will accrue on such shares of Series A Preferred Stock, subject to adjustment in the event of any stock split, stock dividend, or other similar recapitalization with respect to the Series A Preferred Stock (the "Series A Accruing Dividends", and together with the Series B Accruing Dividends, the "Accruing Dividends"). The Accruing Dividends are cumulative and are payable only when and if declared by the board of directors of the Company or in the event of a liquidation, dissolution or winding up of the Company or a Deemed Liquidation Event. The Company cannot declare dividends on the Common Stock unless the holders of Preferred Stock first receive, or simultaneously receive, a dividend on each outstanding share of Preferred Stock. No dividends have been declared since inception.

Liquidation Preference

In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company or Deemed Liquidation Event, the holders of shares of Preferred Stock then outstanding will be entitled to be paid out of the assets of the Company available for distribution to its stockholders before any payment will be made to the holders of Common Stock by reason of their ownership thereof, an amount per share equal to the greater of (i) the applicable Original Issue Price, plus any applicable Accruing Dividends accrued but unpaid thereon, whether or not declared, together with any other dividends declared but unpaid thereon or (ii) such amount per share as would have been payable had all shares of Preferred Stock been

Fulcrum Therapeutics, Inc.**Notes to Consolidated Financial Statements (Continued)****6. Convertible Preferred Stock (Continued)**

converted into Common Stock immediately prior to such liquidation, dissolution, winding up or Deemed Liquidation Event.

After the payment of all preferential amounts required to be paid to the holders of shares of Preferred Stock, the remaining assets of the Company available for distribution to its stockholders will be distributed among the holders of the shares of Common Stock, pro rata based on the number of shares held by each such holder.

Unless the holders of at least 65% of the outstanding shares of Preferred Stock, voting together as a single class, elect otherwise, a "Deemed Liquidation Event" will include (i) a merger or consolidation (other than one in which stockholders of the Company owning a majority by voting power of the outstanding shares of the Company prior to the merger or consolidation continue to own a majority by voting power of the outstanding shares of the surviving or acquiring corporation) or (ii) a sale, lease, transfer, exclusive license, or other disposition by the Company or its subsidiaries of all or substantially all of the assets of the Company and its subsidiaries, taken as a whole, or the sale or disposition of one or more subsidiaries of the Company if substantially all of the assets of the Company and its subsidiaries, taken as a whole, are held by such subsidiaries.

7. Common Stock

Each share of Common Stock entitles the holder to one vote on all matters submitted to a vote of the Company's stockholders provided, however, that, except as otherwise required by law, holders of Common Stock will not be entitled to vote on any amendment to the Company's Certificate of Incorporation that relates solely to the terms of one or more outstanding series of Preferred Stock if the holders of such affected series are entitled, either separately or together with the holders of one or more other such series, to vote thereon pursuant to the Certificate of Incorporation or pursuant to the Delaware General Corporation Law. Common stockholders are entitled to receive dividends, as may be declared by the Company's board of directors, if any, subject to the preferential dividend rights of the Preferred Stock. No dividends have been declared or paid during the years ended December 31, 2017 or 2018.

During the year ended December 31, 2018, the Company's Certificate of Incorporation was amended and restated to increase the number of authorized shares of Common Stock from 80,000,000 to 135,000,000 shares.

The Company had reserved the following shares of Common Stock for the potential conversion of Preferred Stock and for the future issuance of Common Stock pursuant to the Company's 2016 Stock Incentive Plan, as amended from time to time (the "2016 Plan"):

	December 31, 2017	December 31, 2018
Shares reserved for conversion of outstanding Series A Preferred Stock	60,000,000	60,000,000
Shares reserved for conversion of outstanding Series B Preferred Stock	—	40,000,000
Shares reserved for future issuance under the 2016 Stock Incentive Plan	1,542,195	6,432,941
	<u>61,542,195</u>	<u>106,432,941</u>

Fulcrum Therapeutics, Inc.

Notes to Consolidated Financial Statements (Continued)

8. Stock-based Compensation Expense

Grants Under the 2016 Stock Incentive Plan

In July 2016, the Company adopted the 2016 Plan, under which it may grant restricted stock awards, restricted stock units, incentive stock options, non-statutory stock options and other stock-based awards to eligible employees, officers, directors, consultants and advisors.

The 2016 Plan is administered by the board of directors or, at the discretion of the board of directors, by a subcommittee of the board of directors. The exercise prices, vesting and other restrictions are determined at the discretion of the board of directors, or their subcommittee if so delegated, except that the exercise price per share of the stock options may not be less than 100% of the fair market value of a share of the Company's Common Stock on the date of grant and the term of the stock options may not be greater than ten years.

During the year ended December 31, 2018, the Company granted restricted stock awards and stock options. As of December 31, 2017, the Company had only granted restricted stock awards since its inception. The dates of the Company's valuations of Common Stock have not always coincided with the dates of the restricted stock awards. For financial reporting purposes, the Company performed Common Stock valuations with the assistance of a third-party specialist as of November 30, 2018, August 24, 2018, June 1, 2018, December 31, 2017 and December 31, 2016 to determine stock-based compensation expense for restricted stock awards and stock options.

The total number of shares of Common Stock that were authorized for issuance under the 2016 Plan was 12,465,000 as of December 31, 2017. In January 2018, the 2016 Plan was amended to increase the number of shares of Common Stock reserved for issuance under the 2016 Plan by 3,000,000 shares. In August 2018, the 2016 Plan was amended to increase the number of shares of Common Stock reserved for issuance under the 2016 Plan by 7,000,000 shares. The total number of shares of Common Stock that were authorized for issuance under the 2016 Plan was 22,465,000 as of December 31, 2018. Refer to Note 14 for an additional increase to the number of shares issuable under the 2016 Plan that occurred subsequent to December 31, 2018.

During the year ended December 31, 2017, the Company issued 3,628,805 shares and 40,000 shares of Common Stock to employees and non-employees, respectively, under the 2016 Plan. During the year ended December 31, 2018, the Company issued 1,797,013 shares of Common Stock to employees under the 2016 Plan. The Company may repurchase unvested shares at the original purchase price if employees or non-employees are terminated or cease their employment or service relationship with the Company. The shares typically vest over a one-year or four-year period. The shares are recorded in stockholders' (deficit) equity as they vest.

Fulcrum Therapeutics, Inc.

Notes to Consolidated Financial Statements (Continued)

8. Stock-based Compensation Expense (Continued)

The following table summarizes the Company's restricted stock activity under the 2016 Plan:

	Number of Shares	Weighted Average Grant Date Fair Value
Unvested at December 31, 2016	6,631,980	\$ 0.42
Granted	3,668,805	0.44
Vested	(2,561,582)	0.42
Repurchased	(56,250)	0.42
Unvested at December 31, 2017	7,682,953	\$ 0.43
Granted	1,797,013	0.48
Vested	(3,524,983)	0.44
Repurchased	(655,980)	0.46
Unvested at December 31, 2018	<u>5,299,003</u>	\$ 0.44

Shares of Common Stock repurchased from employees and non-employees are shares held in the Company's treasury ("Treasury Shares"). The board of directors may, at its discretion, authorize that the Treasury Shares be returned to the pool of authorized but unissued Common Stock.

Stock options granted by the Company typically vest over a four year period and have a ten year contractual term. The following table summarizes the Company's stock option activity under the 2016 Plan since December 31, 2017:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value
Outstanding at December 31, 2017	—	\$ —	—	\$ —
Granted	3,555,302	1.02		
Exercised	—	—		
Cancelled	—	—		
Outstanding at December 31, 2018	<u>3,555,302</u>	\$ 1.02	9.84	\$ 367,427
Exercisable at December 31, 2018	<u>102,694</u>	\$ 0.68	9.48	\$ 44,158

The aggregate intrinsic value of stock options is calculated as the difference between the exercise price of the stock options and the fair value of the Company's Common Stock as of the balance sheet date for those options that had exercise prices lower than the fair value of the Company's Common Stock.

The weighted average grant date fair value of stock options granted in the year ended December 31, 2018 was \$0.72 per share. As of December 31, 2018, no stock options have been exercised since inception.

Fulcrum Therapeutics, Inc.**Notes to Consolidated Financial Statements (Continued)****8. Stock-based Compensation Expense (Continued)**

The fair value of stock options granted during the year ended December 31, 2018 under the 2016 Plan has been calculated on the date of grant using the following weighted average assumptions:

	<u>Year Ended</u> <u>December 31, 2018</u>
Risk-free interest rate	2.8%
Expected dividend yield	0.0%
Expected term (years)	6.1
Expected stock price volatility	81.6%

Grants Outside the 2016 Stock Incentive Plan

During July 2016, the Company issued 5,075,000 shares and 460,000 shares of Common Stock outside of the Company's 2016 Plan to non-employee founders and certain advisors, respectively. The shares were issued under the terms of restricted stock agreements between the Company and such holders, and the unvested shares are subject to repurchase by the Company upon the termination of the holder's relationship with the Company. Of the total shares issued to non-employee founders, 575,000 vested immediately upon grant; 2,500,000 vest quarterly over a four-year period based on each holder's continued service relationship with the Company; and 2,000,000 vest in equal quarterly installments over a period of one year, commencing with the first quarter after the four-year anniversary of the date of the respective non-employee founder's agreement, based on each holder's continued service relationship with the Company. Of the shares issued to non-employee advisors, 240,000 shares vest in equal quarterly installments over four years, 200,000 of the shares vest in equal quarterly installments over a period of two years upon the achievement of certain performance-based milestones, and 20,000 shares vested immediately upon grant. Stock-based compensation expense associated with the performance-based awards is recognized if the performance condition is considered probable of achievement using management's best estimates.

During the year ended December 31, 2017, management concluded that the milestone associated with 200,000 shares of performance-based restricted stock was probable of achievement, and therefore the Company began to record stock-based compensation expense using the accelerated attribution method. The milestone was subsequently achieved during the year ended December 31, 2018. The Company recorded \$0.1 million and less than \$0.1 million of stock-based compensation expense for non-employee performance-based awards during the years ended December 31, 2017 and 2018, respectively. The shares are recorded in stockholders' (deficit) equity as they vest.

Fulcrum Therapeutics, Inc.**Notes to Consolidated Financial Statements (Continued)****8. Stock-based Compensation Expense (Continued)**

The following table summarizes the Company's restricted stock activity outside of the 2016 Plan:

	Number of Shares	Weighted Average Grant Date Fair Value
Unvested at December 31, 2016	4,597,500	\$ 0.42
Granted	—	—
Vested	(685,000)	0.42
Repurchased	—	—
Unvested at December 31, 2017	3,912,500	\$ 0.42
Granted	—	—
Vested	(785,000)	0.42
Repurchased	—	—
Unvested at December 31, 2018	<u>3,127,500</u>	\$ 0.42

The aggregate intrinsic value of all restricted stock awards that vested during the years ended December 31, 2017 and 2018 was \$1.5 million and \$3.4 million, respectively.

Stock-based Compensation Expense

The total compensation cost recognized in the statements of operations associated with all stock-based compensation awards granted by the Company is as follows (in thousands):

	Year Ended December 31, 2017	Year Ended December 31, 2018
Research and development	\$ 804	\$ 1,124
General and administrative	567	1,035
Total stock-based compensation expense	<u>\$ 1,371</u>	<u>\$ 2,159</u>

As of December 31, 2018, the Company had an aggregate of \$5.6 million of unrecognized stock-based compensation expense, which is expected to be recognized over a weighted average period of 2.94 years.

9. Commitments and Contingencies**Operating Leases**

In May 2016, the Company entered into a sublease agreement for approximately 8,143 square feet of office and laboratory space at its prior corporate headquarters in Cambridge, Massachusetts. The sublease commenced during June 2016. The Company had the option to extend the sublease until June 30, 2019, subject to the landlord's own need for the space. During June 2017, the Company exercised its option to extend the sublease through June 30, 2019. During February 2018, the Company amended its sublease agreement to reduce the term of the sublease to June 30, 2018. The Company recorded rent expense for this sublease on a straight-line basis. Rent expense associated with this sublease for the years ended December 31, 2017 and 2018 was \$0.5 million and \$0.3 million, respectively. The sublease for this space terminated on June 30, 2018.

Fulcrum Therapeutics, Inc.**Notes to Consolidated Financial Statements (Continued)****9. Commitments and Contingencies (Continued)**

In November 2017, the Company entered into a lease agreement for its current corporate headquarters for approximately 28,731 square feet of office and laboratory space in Cambridge, Massachusetts, commencing December 2017. The Company began recognizing rent expense associated with this lease during December 2017. The Company began to occupy and use the leased space for its intended purpose in June 2018. The lease ends on June 30, 2028. The Company has the option to extend the term of the lease for an additional five-year period, at the market rate, by giving the landlord written notice of its election to exercise the extension at least nine months prior to the original expiration of the lease term. The lease has a total commitment of \$25.1 million over the ten year term, and includes escalating rent payments. The lease provides the Company with an allowance for normal leasehold improvements of \$5.0 million. The Company accounts for leasehold improvement incentives as a reduction to rent expense ratably over the lease term. The balance from the leasehold improvement incentives is classified as a deferred lease incentive on the balance sheet. As of December 31, 2017, the Company had not incurred leasehold improvement costs that are subject to reimbursement by the landlord, and therefore no lease incentive obligation was recorded on the balance sheet. The lease agreement requires the Company to either pay a security deposit or maintain a letter of credit of \$1.1 million. The Company obtained a letter of credit for this lease in April 2018 and has recorded the cash held to secure the letter of credit as restricted cash on the consolidated balance sheet as of December 31, 2018. The Company records rent expense for this lease on a straight-line basis. Rent expense associated with this lease for the years ended December 31, 2017 and 2018 was approximately \$0.2 million and \$1.9 million, respectively.

The future minimum lease payments associated with the lease for the Company's current headquarters as of December 31, 2018 are as follows (in thousands):

2019	\$ 2,219
2020	2,285
2021	2,354
2022	2,424
2023	2,497
Thereafter	12,187
Total minimum lease payments	<u>\$ 23,966</u>

Other Agreements

The Company has agreements with third parties in the normal course of business under which it can license certain developed technologies. If the Company exercises its rights to license the technologies it may be subject to additional fees and milestone payments. As of December 31, 2018, the Company has not exercised its rights to license such technologies.

Indemnification Agreements

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, business partners and other parties with respect to certain matters arising out of the relationship between such parties and the Company. In addition, the Company has entered into indemnification agreements with members of its board of directors and senior management that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers. The maximum potential amount of future

Fulcrum Therapeutics, Inc.**Notes to Consolidated Financial Statements (Continued)****9. Commitments and Contingencies (Continued)**

payments the Company could be required to make under these indemnification agreements is, in many cases, unlimited. To date, the Company has not incurred any material costs as a result of such indemnifications. The Company is not aware of any claims under indemnification arrangements, and it has not accrued any liabilities related to such obligations as of December 31, 2017 or 2018.

Legal Proceedings

The Company is not currently a party to any material legal proceedings. At each reporting date, the Company evaluates whether or not a potential loss amount or a potential range of loss is probable and reasonably estimable under the provisions of the authoritative guidance that addresses accounting for contingencies. The Company expenses the costs related to its legal proceedings as they are incurred. No such costs have been incurred for the years ended December 31, 2017 and 2018.

10. Income Taxes

A reconciliation of the U.S. federal statutory income tax rate to the Company's effective income tax rate is as follows:

	Year Ended December 31, 2017	Year Ended December 31, 2018
Federal income tax (benefit) at statutory rate	34.00%	21.00%
Permanent differences	(3.64)	(1.37)
Federal and state research and development credits	4.81	3.15
State income tax, net of federal benefit	4.88	5.77
Impact of U.S. tax reform	(16.25)	—
Change in valuation allowance	(23.80)	(28.55)
Effective income tax rate	—%	—%

During the years ended December 31, 2017 and 2018, the Company incurred book and tax losses and, because it maintains a full valuation allowance on its net deferred tax assets, did not recognize federal or state income tax expense or benefit.

Fulcrum Therapeutics, Inc.**Notes to Consolidated Financial Statements (Continued)****10. Income Taxes (Continued)**

The Company's deferred tax assets and liabilities consist of the following (in thousands):

	<u>December 31, 2017</u>	<u>December 31, 2018</u>
Deferred tax assets:		
Net operating loss carryforwards	\$ 8,493	\$ 16,566
Research and development credit carryforwards	1,475	2,503
Accrued expenses and other	336	457
Deferred lease incentive	—	1,218
Deferred rent	54	383
Gross deferred tax assets	<u>10,358</u>	<u>21,127</u>
Valuation allowance	<u>(10,293)</u>	<u>(19,592)</u>
Net deferred tax assets	65	1,535
Deferred tax liability	<u>(65)</u>	<u>(1,535)</u>
Net deferred tax assets	<u>\$ —</u>	<u>\$ —</u>

The Company has evaluated the positive and negative evidence bearing upon its ability to realize the deferred tax assets. The Company considered its history of cumulative net losses incurred since inception and its lack of commercialization of any products since inception and has concluded that it is more likely than not that the Company will not realize the benefits of the deferred tax assets. Accordingly, a full valuation allowance has been established against the net deferred tax assets as of December 31, 2017 and 2018. The Company reevaluates the positive and negative evidence at each reporting period.

As of December 31, 2018, the Company had federal net operating loss carryforwards of approximately \$60.7 million which begin to expire in 2035. Approximately \$29.7 million of the federal net operating losses can be carried forward indefinitely. As of December 31, 2018, the Company also had state net operating loss carryforwards of approximately \$60.5 million, which begin to expire in 2035.

As of December 31, 2018, the Company had federal research and development tax credit carryforwards of approximately \$1.5 million, which begin to expire in 2035. As of December 31, 2018, the Company also had state research and development tax credit carryforwards of approximately \$1.3 million, which begin to expire in 2035.

Utilization of the net operating loss carryforwards and research and development tax credit carryforwards may be subject to an annual limitation under Section 382 of the Internal Revenue Code of 1986, as amended (the "Internal Revenue Code"), and corresponding provisions of state law, due to ownership changes that have occurred previously or that could occur in the future. These ownership changes may limit the amount of carryforwards that can be utilized annually to offset future taxable income. In general, an ownership change, as defined by Section 382, results from transactions increasing the ownership of certain shareholders or public groups in the stock of a corporation by more than 50% over a three-year period. The Company has not conducted a study to assess whether a change of control has occurred or whether there have been multiple changes of control since inception due to the significant complexity and cost associated with such a study. If the Company has experienced a change of control, as defined by Section 382, at any time since inception, utilization of the net operating loss carryforwards or research and development tax credit carryforwards would be subject to an annual limitation under Section 382, which is determined by first multiplying the value of the Company's stock at the time of the ownership change by the applicable long-term tax-exempt rate, and then could be subject to additional

Fulcrum Therapeutics, Inc.

Notes to Consolidated Financial Statements (Continued)

10. Income Taxes (Continued)

adjustments, as required. Any limitation may result in expiration of a portion of the net operating loss carryforwards or research and development tax credit carryforwards before utilization. Further, until a study is completed and any limitation is known, no amounts are being presented as an uncertain tax position.

The Company files tax returns as prescribed by the tax laws of the jurisdictions in which it operates. In the normal course of business, the Company is subject to examination by federal and state jurisdictions, where applicable. There are currently no pending tax examinations. As of December 31, 2018, the Company's tax years are still open under statute from 2015 to the present.

It is the Company's policy to include penalties and interest expense related to income taxes as a component of the provision for income taxes. As of December 31, 2017 and 2018, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in the Company's statements of operations. For the year ended December 31, 2018, the Company generated research credits but has not conducted a study to document the qualified activities. This study may result in an adjustment to the Company's research and development credit carryforwards; however, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company's research and development credits and, if an adjustment is required, this adjustment would result in an adjustment to the deferred tax asset established for the research and development credit carryforwards and the valuation allowance.

On December 22, 2017, the Tax Cuts and Jobs Act (the "Tax Reform Act") was enacted, which significantly reforms the Internal Revenue Code. The Tax Reform Act, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, effective as of January 1, 2018; limitation of the tax deduction for interest expense; limitation of the deduction for net operating losses to 80% of annual taxable income and elimination of net operating loss carrybacks, in each case, for losses arising in taxable years beginning after December 31, 2017 (though any such tax losses may be carried forward indefinitely); and modifying or repealing many business deductions and credits, including reducing the business tax credit for certain clinical testing expenses incurred in the testing of certain drugs for rare diseases or conditions generally referred to as "orphan drugs."

The staff of the Securities and Exchange Commission issued Staff Accounting Bulletin No. 118 ("SAB 118") to address the application of GAAP in situations when a registrant does not have the necessary information available, prepared, or analyzed (including computations) in reasonable detail to complete the accounting for certain income tax effects of the Tax Reform Act. The Company is applying the provisions of SAB 118. In connection with the initial analysis of the impact of the Tax Reform Act for the year ended December 31, 2017, the Company remeasured certain deferred tax assets and liabilities based on the revised U.S. federal corporate tax rate of 21%. The remeasurement of the Company's deferred tax assets and liabilities was offset by a corresponding change in the Company's valuation allowance.

As permitted by SAB 118, the Company recorded provisional estimates during the year ended December 31, 2017 and has subsequently finalized its accounting analysis based on the guidance, interpretations, and data available as of December 31, 2018. Adjustments made in the fourth quarter of 2018 upon finalization of the Company's accounting analysis were not material to the Company's consolidated financial statements.

Fulcrum Therapeutics, Inc.**Notes to Consolidated Financial Statements (Continued)****11. Defined Contribution Plan**

The Company has a defined contribution savings plan under Section 401(k) of the Internal Revenue Code (the "401(k) Plan"). The 401(k) Plan covers all employees who meet defined minimum age and service requirements, and allows participants the option to elect to defer a portion of their annual compensation on a pretax basis. As currently established, the Company is not required to make and has not made any contributions to the 401(k) Plan.

12. Net Loss per Share and Unaudited Pro Forma Net Loss per Share***Net Loss per Share***

Basic net loss per share attributable to common stockholders is calculated by dividing net loss attributable to common stockholders by the weighted average shares outstanding during the period, without consideration for Common Stock equivalents. Net loss attributable to common stockholders is calculated by adjusting the net loss of the Company for cumulative preferred stock dividends. Diluted net loss per share attributable to common stockholders is calculated by adjusting weighted average shares outstanding for the dilutive effect of Common Stock equivalents outstanding for the period. For purposes of the diluted net loss per share attributable to common stockholders calculation, Preferred Stock, stock options, and unvested restricted stock are considered to be Common Stock equivalents but are excluded from the calculation of diluted net loss per share attributable to common stockholders, as their effect would be anti-dilutive. Therefore, basic and diluted net loss per share attributable to common stockholders were the same for all periods presented as a result of the Company's net loss.

The following Common Stock equivalents were excluded from the calculation of diluted net loss per share attributable to common stockholders for the periods indicated because including them would have had an anti-dilutive effect:

	<u>Year Ended December 31, 2017</u>	<u>Year Ended December 31, 2018</u>
Series A Preferred Stock	34,666,667	60,000,000
Series B Preferred Stock	—	40,000,000
Outstanding stock options	—	3,555,302
Unvested restricted stock awards	11,595,453	8,426,503
Total	<u><u>46,262,120</u></u>	<u><u>111,981,805</u></u>

In February 2019, the Company issued 12,500,000 shares of Series B Preferred Stock as consideration for the GSK Agreement (as defined in Note 14).

Unaudited Pro Forma Net Loss per Share

The unaudited pro forma basic and diluted net loss per share attributable to common stockholders for the year ended December 31, 2018 give effect to adjustments arising upon the closing of a qualified IPO. The unaudited pro forma basic and diluted weighted average common shares outstanding used in the calculation of unaudited pro forma basic and diluted net loss per share attributable to common stockholders for the year ended December 31, 2018 give effect to the automatic conversion upon a qualified IPO of all outstanding shares of Preferred Stock into shares of Common Stock as if the conversion had occurred on the later of January 1, 2018 or the issuance date of the Preferred Stock. Accordingly, the pro forma basic and diluted net loss per share attributable to stockholders does not include the effects of the cumulative preferred stock dividends. Shares to be sold in the offering are

Fulcrum Therapeutics, Inc.**Notes to Consolidated Financial Statements (Continued)****12. Net Loss per Share and Unaudited Pro Forma Net Loss per Share (Continued)**

excluded from the unaudited pro forma basic and diluted loss per share attributable to common stockholders calculations.

The following table summarizes the Company's unaudited pro forma net loss per share attributable to common stockholders (in thousands, except per share data):

	<u>Year Ended</u> <u>December 31, 2018</u>
Numerator:	
Net loss attributable to common stockholders	\$ (39,147)
Cumulative convertible preferred stock dividends	6,559
Pro forma net loss attributable to common stockholders	<u>\$ (32,588)</u>
Denominator:	
Weighted average common shares outstanding	8,799
Pro forma weighted average shares outstanding after giving effect to the conversion of Preferred Stock	67,856
Pro forma weighted average shares outstanding	<u>76,655</u>
Pro forma basic and diluted loss per share attributable to common stockholders, basic and diluted	<u>\$ (0.43)</u>

13. Related-Party Transactions

During the years ended December 31, 2017 and 2018, the Company paid fees to Third Rock Ventures, LLC ("TRV"), an affiliate of one of the Company's principal stockholders, in exchange for consulting services. The Company recorded expenses related to such fees of \$0.1 million during each of the years ended December 31, 2017 and 2018. As of both December 31, 2017 and 2018, there was less than \$0.1 million of amounts due to TRV for such services that were included in accounts payable and accrued expenses. Additionally, consultants that provide services to the Company are employees of TRV. The Company has issued an aggregate of 996,000 shares of Common Stock to these consultants in exchange for their continuing consulting services.

During the year ended December 31, 2018, the Company recorded other income of \$0.4 million related to the sale of drug material to an entity affiliated with TRV.

14. Subsequent Events

For its consolidated financial statements as of December 31, 2018 and for the year then ended, the Company evaluated subsequent events through May 1, 2019, the date on which those consolidated financial statements were issued.

2016 Stock Incentive Plan

In January 2019, the 2016 Plan was amended to increase the number of shares of Common Stock reserved for issuance under the 2016 Plan by 2,500,000 shares. In January 2019 and March 2019, the Company issued stock options to purchase an aggregate of 7,143,661 shares of Common Stock under the 2016 Plan.

Fulcrum Therapeutics, Inc.**Notes to Consolidated Financial Statements (Continued)****14. Subsequent Events (Continued)*****GSK Agreement***

In February 2019, the Company entered into a right of reference and license agreement (the "GSK Agreement") with subsidiaries of GlaxoSmithKline plc (collectively referred to as "GSK"), pursuant to which the Company has been granted an exclusive worldwide license to develop and commercialize losmapimod. Under the GSK Agreement, the Company also acquired reference rights to relevant regulatory and manufacturing documents and GSK's existing supply of losmapimod drug substance and product. The Company also has the right to sublicense its rights under the license agreement, subject to certain conditions. The Company is obligated to use commercially reasonable efforts to develop and commercialize losmapimod at its sole cost. The Company is also responsible for costs related to the filing and maintenance of the licensed patent rights.

Under the GSK Agreement, the Company issued 12,500,000 million shares of Series B Preferred Stock to GSK with an estimated fair value of \$25.5 million, or \$2.04 per share, which was determined with the assistance of a third-party specialist contemporaneously with the issuance of the Series B Preferred Stock to GSK. In addition, the Company may owe GSK up to \$37.5 million in certain specified clinical and regulatory milestones, of which \$2.5 million is due upon the initiation of a Phase 2 clinical trial, and up to \$60.0 million in certain specified sales milestones. The Company has agreed to pay tiered royalties on annual net sales of losmapimod that range from mid single-digit percentages to a low double-digit, but less than teens, percentage. The royalties are payable on a product-by-product and country-by-country basis, and may be reduced in specified circumstances. The Company also incurred \$0.1 million of direct expenses related to the transaction, which the Company will include in the total consideration for the transaction.

The GSK Agreement may be terminated by either party for a material breach by the other, subject to notice and cure provisions. Unless earlier terminated, the GSK Agreement will continue in effect until the expiration of the Company's royalty obligations, which expire on a country-by-country basis on the later of (i) ten years after the first commercial sale in the country or (ii) approval of a generic version of losmapimod by the applicable regulatory agency.

The Company concluded the arrangement did not result in the acquisition of a business, as substantially all of the fair value of the gross assets acquired was concentrated in a single in-process research and development asset, losmapimod. In addition, the Company did not obtain any substantive processes in connection to the GSK Agreement and losmapimod was not generating revenue at the time the GSK Agreement was executed. Therefore, the Company accounted for the arrangement as an asset acquisition. The Company also concluded that the acquired assets do not have an alternative future use, and therefore the fair value attributable to the GSK Agreement of \$25.6 million, inclusive of transaction costs, will be recorded as in-process research and development expense in the Company's consolidated statement of operations and comprehensive loss for the three months ended March 31, 2019, which is the period in which the Company obtained (i) the license to losmapimod, (ii) the right to reference relevant regulatory and manufacturing documents, and (iii) GSK's existing supply of losmapimod drug substance and product. Additionally, the Company will recognize clinical and regulatory milestone payments when the underlying contingency is resolved and the consideration is paid or becomes payable. The milestone payments will be capitalized or expensed depending on the nature of the associated asset as of the date of recognition. The Company will record sales milestone payments and royalties as additional expense of the related product sales in the period in which the corresponding sales occur.

In February 2019, in connection with the GSK Agreement, the Company's Certificate of Incorporation was amended and restated to increase the number of authorized shares of Series B Preferred Stock from 40,000,000 shares to 52,500,000 shares and to increase the number of authorized shares of Common Stock from 135,000,000 shares to 147,500,000 shares.

Fulcrum Therapeutics, Inc.

Consolidated Balance Sheets

(In thousands, except share and per share amounts)

(Unaudited)

	December 31, 2018	March 31, 2019	Pro Forma March 31, 2019
Assets			
Current assets:			
Cash and cash equivalents	\$ 72,797	\$ 62,452	\$ 62,452
Prepaid expenses and other current assets	1,298	1,544	1,544
Total current assets	74,095	63,996	63,996
Property and equipment, net	10,546	10,225	10,225
Restricted cash	1,092	1,092	1,092
Other assets	38	275	275
Total assets	<u>\$ 85,771</u>	<u>\$ 75,588</u>	<u>\$ 75,588</u>
Liabilities, convertible preferred stock, and stockholders' (deficit) equity			
Current liabilities:			
Accounts payable	\$ 1,263	\$ 2,522	\$ 2,522
Accrued expenses and other current liabilities	2,497	1,699	1,699
Deferred lease incentive, current portion	469	469	469
Total current liabilities	4,229	4,690	4,690
Deferred rent, excluding current portion	1,402	1,450	1,450
Deferred lease incentive, excluding current portion	3,990	3,873	3,873
Other liabilities, excluding current portion	150	126	126
Total liabilities	9,771	10,139	10,139
Commitments and contingencies (Note 10)			
Series A convertible preferred stock, \$0.001 par value; 60,000,000 shares authorized, issued and outstanding as of December 31, 2018 and March 31, 2019 (liquidation preference of \$68,371 as of March 31, 2019); no shares issued or outstanding, pro forma as of March 31, 2019			
	59,909	59,909	—
Series B convertible preferred stock, \$0.001 par value; 40,000,000 and 52,500,000 shares authorized, issued and outstanding as of December 31, 2018 and March 31, 2019, respectively (liquidation preference of \$109,119 as of March 31, 2019); no shares issued or outstanding, pro forma as of March 31, 2019			
	79,761	105,227	—
Stockholders' (deficit) equity:			
Common stock, \$0.001 par value; 135,000,000 and 147,500,000 shares authorized as of December 31, 2018 and March 31, 2019, respectively; 19,542,588 and 19,235,125 shares issued as of December 31, 2018 and March 31, 2019, respectively; 11,116,085 and 12,054,235 shares outstanding as of December 31, 2018 and March 31, 2019, respectively; 131,735,125 and 124,554,235 shares issued and outstanding, pro forma as of March 31, 2019			
	11	12	125
Treasury stock, at cost; 469,169 and no shares as of December 31, 2018 and March 31, 2019, respectively; no shares, pro forma as of March 31, 2019			
	—	—	—
Additional paid-in capital	4,443	5,268	170,291
Accumulated deficit	(68,124)	(104,967)	(104,967)
Total stockholders' (deficit) equity	(63,670)	(99,687)	65,449
Total liabilities, convertible preferred stock, and stockholders' (deficit) equity	<u>\$ 85,771</u>	<u>\$ 75,588</u>	<u>\$ 75,588</u>

The accompanying notes are an integral part of these financial statements.

Fulcrum Therapeutics, Inc.**Consolidated Statements of Operations and Comprehensive Loss****(In thousands, except per share data)****(Unaudited)**

	Three Months Ended	
	March 31,	
	2018	2019
Operating expenses:		
Research and development	\$ 5,573	\$ 34,629
General and administrative	1,737	2,598
Total operating expenses	7,310	37,227
Loss from operations	(7,310)	(37,227)
Other income, net:		
Interest income, net	—	377
Other income	370	7
Net loss and comprehensive loss	<u>\$ (6,940)</u>	<u>\$ (36,843)</u>
Cumulative convertible preferred stock dividends	(828)	(3,041)
Net loss attributable to common stockholders	<u>\$ (7,768)</u>	<u>\$ (39,884)</u>
Net loss per share attributable to common stockholders, basic and diluted	<u>\$ (1.09)</u>	<u>\$ (3.47)</u>
Weighted average number of common shares used in net loss per share attributable to common stockholders, basic and diluted	<u>7,134</u>	<u>11,497</u>
Pro forma net loss per share attributable to common stockholders, basic and diluted		<u>\$ (0.31)</u>
Pro forma weighted average number of common shares used in net loss per share attributable to common stockholders, basic and diluted		<u>118,580</u>

The accompanying notes are an integral part of these financial statements.

Fulcrum Therapeutics, Inc.

Consolidated Statements of Convertible Preferred Stock and Stockholders' (Deficit) Equity

(In thousands, except share amounts)

(Unaudited)

	Series A Convertible Preferred Stock		Series B Convertible Preferred Stock		Common Stock		Treasury Stock		Additional Paid-In Capital	Accumulated Deficit	Total Stockholders' (Deficit) Equity
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount			
Balance at December 31, 2017	34,666,666	\$ 34,587	—	\$ —	6,806,102	\$ 7	56,250	\$ —	\$ 2,264	\$ (35,536)	\$ (33,265)
Issuance of Series A convertible preferred stock at \$1.00 per share, net of issuance costs of \$7	12,666,667	12,659	—	—	—	—	—	—	—	—	—
Issuance of common stock	—	—	—	—	876,019	1	—	—	3	—	4
Repurchase of unvested restricted stock awards	—	—	—	—	—	—	88,194	—	—	—	—
Retirement of treasury shares	—	—	—	—	—	—	(144,444)	—	—	—	—
Stock-based compensation expense	—	—	—	—	—	—	—	—	429	—	429
Net loss	—	—	—	—	—	—	—	—	—	(6,940)	(6,940)
Balance at March 31, 2018	47,333,333	\$ 47,246	—	\$ —	7,682,121	\$ 8	—	\$ —	\$ 2,696	\$ (42,476)	\$ (39,772)
Balance at December 31, 2018	60,000,000	\$ 59,909	40,000,000	\$ 79,761	11,116,085	\$ 11	469,169	\$ —	\$ 4,443	\$ (68,124)	\$ (63,670)
Issuance of Series B convertible preferred stock in connection with asset acquisition, net of issuance costs of \$34	—	—	12,500,000	25,466	—	—	—	—	—	—	—
Issuance of common stock	—	—	—	—	938,150	1	—	—	4	—	5
Repurchase of unvested restricted stock awards	—	—	—	—	—	—	307,463	—	—	—	—
Retirement of treasury shares	—	—	—	—	—	—	(776,632)	—	—	—	—
Stock-based compensation expense	—	—	—	—	—	—	—	—	821	—	821
Net loss	—	—	—	—	—	—	—	—	—	(36,843)	(36,843)
Balance at March 31, 2019	60,000,000	\$ 59,909	52,500,000	\$ 105,227	12,054,235	\$ 12	—	\$ —	\$ 5,268	\$ (104,967)	\$ (99,687)
Pro forma convertible preferred stock and stockholders' equity (unaudited):											
Conversion of convertible preferred stock into common stock	(60,000,000)	(59,909)	(52,500,000)	(105,227)	112,500,000	113	—	—	165,023	—	165,136
Pro forma balance at March 31, 2019	—	\$ —	—	\$ —	124,554,235	\$ 125	—	\$ —	\$ 170,291	\$ (104,967)	\$ 65,449

The accompanying notes are an integral part of these financial statements.

Fulcrum Therapeutics, Inc.
Consolidated Statements of Cash Flows
(In thousands)
(Unaudited)

	Three Months Ended	
	March 31,	
	2018	2019
Operating activities		
Net loss	\$ (6,940)	\$ (36,843)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation expense	174	504
Stock-based compensation expense	429	821
In-process research and development expenses	—	25,591
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(565)	(264)
Other assets	28	(63)
Accounts payable	196	1,233
Accrued expenses and other current liabilities	(430)	(807)
Deferred rent and deferred lease incentive	476	(69)
Net cash used in operating activities	(6,632)	(9,897)
Investing activities		
Purchases of property and equipment	(783)	(310)
Transaction costs associated with asset acquisition	—	(91)
Net cash used in investing activities	(783)	(401)
Financing activities		
Proceeds from issuance of Series A convertible preferred stock, net of issuance costs	12,665	—
Issuance costs associated with issuance of Series B convertible preferred stock	—	(34)
Principal payments on capital lease obligations	(42)	(11)
Proceeds from issuance of common stock (repurchases of common stock)	17	(2)
Net cash provided by (used in) financing activities	12,640	(47)
Net increase (decrease) in cash, cash equivalents and restricted cash	5,225	(10,345)
Cash, cash equivalents, and restricted cash, beginning of period	407	73,889
Cash, cash equivalents, and restricted cash, end of period	\$ 5,632	\$ 63,544
Supplemental cash flow information		
Cash paid for interest	\$ 2	\$ 2
Non-cash investing and financing activities:		
Acquisition of in process research and development through issuance of stock	\$ —	\$ 25,500
Property and equipment purchases unpaid at end of period	\$ 1,778	\$ 47
Deferred offering costs unpaid at end of period	\$ —	\$ 190

The following table provides a reconciliation of the cash, cash equivalents, and restricted cash balances as of each of the periods shown above:

	March 31, 2018	March 31, 2019
Cash and cash equivalents	\$ 5,632	\$ 62,452
Restricted cash	—	1,092
Total cash, cash equivalents, and restricted cash	\$ 5,632	\$ 63,544

The accompanying notes are an integral part of these financial statements.

Fulcrum Therapeutics, Inc.

Notes to Consolidated Financial Statements

1. Nature of the Business and Basis of Presentation

Fulcrum Therapeutics, Inc. (the "Company" or "Fulcrum") was incorporated in Delaware on August 18, 2015. The Company is focused on improving the lives of patients with genetically defined diseases in areas of high unmet medical need, with an initial focus on rare diseases.

The Company is subject to a number of risks similar to other companies in the biotechnology industry, including, but not limited to, risks of failure of preclinical studies and clinical trials, dependence on key personnel, protection of proprietary technology, reliance on third party organizations, risks of obtaining regulatory approval for any product candidate that it may develop, development by competitors of technological innovations, compliance with government regulations, and the need to obtain additional financing. Product candidates currently under development will require significant additional research and development efforts, including extensive preclinical and clinical testing and regulatory approval, prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel infrastructure and extensive compliance-reporting capabilities. Even if the Company's development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

Basis of Presentation

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Updates ("ASU") of the Financial Accounting Standards Board ("FASB").

The accompanying unaudited consolidated financial statements and footnotes to the financial statements have been prepared on the same basis as the most recently audited annual financial statements and, in the opinion of management, reflect all normal recurring adjustments necessary for the fair presentation of the Company's financial position as of March 31, 2019 and the results of its operations and its cash flows for the three months ended March 31, 2018 and 2019. The results for the three months ended March 31, 2019 are not necessarily indicative of results to be expected for the year ending December 31, 2019, any other interim periods, or any future year or period. These consolidated financial statements should be read in conjunction with the Company's audited consolidated financial statements.

Going Concern

The Company has incurred recurring losses and negative cash flows from operations since inception and has primarily funded its operations with proceeds from the issuance of convertible notes and convertible preferred stock. As of March 31, 2019, the Company had an accumulated deficit of \$105.0 million. The Company expects its operating losses and negative operating cash flows to continue into the foreseeable future as it continues to expand its research and development efforts. As of June 5, 2019, the issuance date of the consolidated financial statements for the three months ended March 31, 2019, the Company expected that its cash and cash equivalents as of March 31, 2019 will be sufficient to fund its operating expenses and capital expenditure requirements into the first quarter of 2020. The future viability of the Company beyond that point is dependent on its ability to raise additional capital to finance its operations.

If the Company is unable to obtain additional funding, the Company could be forced to delay, reduce or eliminate some or all of its research and development programs, product portfolio expansion, or

Fulcrum Therapeutics, Inc.

Notes to Consolidated Financial Statements (Continued)

1. Nature of the Business and Basis of Presentation (Continued)

commercialization efforts, which could adversely affect its business prospects, or the Company may be unable to continue operations. The Company is seeking to complete an initial public offering ("IPO") of its common stock ("Common Stock"). In the event the Company does not complete an IPO, the Company expects to seek additional funding through private equity financings, debt financings, or other capital sources, including collaborations with other companies or other strategic transactions. Although management plans to pursue additional funding, there is no assurance that the Company will be successful in obtaining sufficient funding on terms acceptable to the Company to fund continuing operations, if at all.

Based on its recurring losses and negative cash flows from operations since inception, expectation of continuing operating losses and negative cash flows from operations for the foreseeable future, and the need to raise additional capital to finance its future operations, management concluded that there is substantial doubt about the Company's ability to continue as a going concern within one year after the date that the consolidated financial statements as of and for the three months ended March 31, 2019 were issued.

The accompanying consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty. Accordingly, the consolidated financial statements have been prepared on a basis that assumes the Company will continue as a going concern and which contemplates the realization of assets and satisfaction of liabilities and commitments in the ordinary course of business.

2. Summary of Significant Accounting Policies

Principles of Consolidation

The accompanying consolidated financial statements include the accounts of the Company and its wholly owned subsidiary, Fulcrum Therapeutics Securities Corp., which is a Massachusetts subsidiary created to buy, sell, and hold securities. All intercompany transactions and balances have been eliminated.

Summary of Significant Accounting Policies

The significant accounting policies and estimates used in the preparation of the consolidated financial statements are described in the Company's audited financial statements. There have been no material changes in the Company's significant accounting policies during the three months ended March 31, 2019.

Use of Estimates

The preparation of financial statements in accordance with GAAP requires management to make certain estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities as of the date of the financial statements, and the reported amount of expenses during the reported periods. Estimates inherent in the preparation of these consolidated financial statements include, but are not limited to, estimates related to accrued expenses, stock-based compensation expense, the fair value of the Common Stock and convertible preferred stock, and income taxes. The Company bases its estimates on historical experience and other market specific or other relevant assumptions it believes to be reasonable under the circumstances. On an ongoing basis, management evaluates its estimates as there are changes in circumstances, facts and experience. Actual results could differ from those estimates or assumptions.

Fulcrum Therapeutics, Inc.**Notes to Consolidated Financial Statements (Continued)****2. Summary of Significant Accounting Policies (Continued)*****Pro Forma Financial Information***

The accompanying pro forma balance sheet and statement of stockholders' (deficit) equity as of March 31, 2019 has been prepared to give effect, upon the closing of a qualified IPO, to the automatic conversion of all shares of convertible preferred stock outstanding as of March 31, 2019 into 112,500,000 shares of Common Stock. In the accompanying consolidated statements of operations and comprehensive loss, the pro forma basic and diluted net loss per share attributable to common stockholders for the three months ended March 31, 2019 have been prepared to give effect, upon the closing of a qualified IPO, to the automatic conversion of all outstanding shares of convertible preferred stock as if the proposed IPO had occurred on the later of January 1, 2019 or the issuance date of the convertible preferred stock (see Note 12).

Deferred Issuance Costs

The Company capitalizes certain legal, professional, accounting and other third-party fees that are directly associated with in-process equity issuances as deferred issuance costs until such equity issuances are consummated. After consummation of the equity issuance, these costs are recorded as a reduction in the capitalized amount associated with the equity issuance. Should the planned financing be abandoned, the deferred issuance costs will be expensed immediately as a charge to operating expenses in the consolidated statement of operations and comprehensive loss. Deferred issuance costs as of December 31, 2018 and March 31, 2019 were less than \$0.1 million and \$0.2 million, respectively.

Research and Development Expenses

Research and development expenses include costs directly attributable to the conduct of research and development programs, including personnel-related expenses such as salaries, payroll taxes, benefits, and stock-based compensation expense, manufacturing and external costs related to outside vendors engaged to conduct both preclinical studies and clinical trials, laboratory supplies, depreciation on and maintenance of research equipment, and the allocable portions of facility costs, such as rent, utilities, repairs and maintenance, depreciation, and general support services. Expenditures relating to research and development are expensed in the period incurred. Nonrefundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

Research and development expenses also include in-process research and development ("IPR&D") expenses, which relate to IPR&D acquired as part of an asset acquisition for which there is no alternative future use. Research and development with no future alternative use is expensed as incurred.

Off-Balance Sheet Risk and Concentrations of Credit Risk

The Company has no significant off-balance sheet risk such as foreign exchange contracts, option contracts, or other foreign hedging arrangements. Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash, cash equivalents, and restricted cash. The Company's cash, cash equivalents, and restricted cash are deposited in accounts at large financial institutions. The Company believes it is not exposed to significant credit risk due to the financial strength of the depository institutions in which the cash, cash equivalents and restricted cash are held. The Company maintains its cash equivalents in money market funds that invest in U.S. Treasury securities.

Fulcrum Therapeutics, Inc.**Notes to Consolidated Financial Statements (Continued)****2. Summary of Significant Accounting Policies (Continued)*****Recent Accounting Pronouncements—To Be Adopted***

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)* ("ASU 2016-02"), as amended by various subsequently issued ASUs. The standard requires lessees to recognize an operating lease with a term greater than one year on their balance sheets as a right-of-use asset and corresponding lease liability, measured at the present value of the lease payments. Lessees are required to classify leases as either finance or operating leases. If the lease is effectively a financed-purchase by the lessee, it is classified as a financing lease, otherwise it is classified as an operating lease. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight-line basis over the term of the lease. In July 2018, the FASB also issued ASU 2018-11, *Leases (Topic 842): Targeted Improvements* ("ASU 2018-11"), which permits entities to continue applying legacy guidance in ASC 840, *Leases*, including its disclosure requirements, in the comparative periods presented in the year that the entity adopts the new leasing standard. The new standard will be effective for the Company on January 1, 2020. The Company will apply the transition method permitted by ASU 2018-11. The Company is currently evaluating the effect that adoption of the standard is expected to have on the Company's consolidated financial statements and related disclosures. The Company expects to take advantage of certain available expedients by electing the transition package of practical expedients permitted within ASU 2016-02, which allows the Company to not reassess previous accounting conclusions around whether arrangements are, or contain, leases, the classification of leases, and the treatment of initial direct costs. The Company also expects to make an accounting policy election to exclude leases with an initial term of twelve months or less from the balance sheet.

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments—Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* ("ASU 2016-13"). The standard requires that credit losses be reported using an expected losses model rather than the incurred losses model that is currently used, and establishes additional disclosures related to credit risks. For available-for-sale debt securities with unrealized losses, this standard requires allowances to be recorded instead of reducing the amortized cost of the investment. The new standard will be effective for the Company on January 1, 2021. The Company is currently evaluating the potential impact that this standard may have on its consolidated financial position and results of operations.

In July 2017, the FASB issued ASU No. 2017-11, *Earnings Per Share (Topic 260), Distinguishing Liabilities from Equity (Topic 480), Derivatives and Hedging (Topic 815) I. Accounting for Certain Financial Instruments with Down Round Features II. Replacement of the Indefinite Deferral for Mandatorily Redeemable Financial Instruments of Certain Nonpublic Entities and Certain Mandatorily Redeemable Noncontrolling Interests with a Scope Exception* ("ASU 2017-11"). Part I of the standard applies to entities that issue financial instruments such as warrants, convertible debt or convertible preferred stock that contain down-round features. Part II of the standard replaces the indefinite deferral for certain mandatorily redeemable noncontrolling interests and mandatorily redeemable financial instruments of nonpublic entities contained within ASC Topic 480 with a scope exception and does not impact the accounting for these mandatorily redeemable instruments. The new standard will be effective for the Company on January 1, 2020. The Company is currently evaluating the impact that the adoption of ASU 2017-11 may have on its consolidated financial statements.

Fulcrum Therapeutics, Inc.**Notes to Consolidated Financial Statements (Continued)****3. Fair Value Measurements**

The following tables present information about the Company's financial assets measured at fair value on a recurring basis and indicate the level of the fair value hierarchy utilized to determine such fair values (in thousands):

	Fair Value Measurements at December 31, 2018			
	Total	Level 1	Level 2	Level 3
Cash equivalents:				
Money market funds	\$ 72,797	\$ 72,797	\$ —	\$ —
Total	<u>\$ 72,797</u>	<u>\$ 72,797</u>	<u>\$ —</u>	<u>\$ —</u>

	Fair Value Measurements at March 31, 2019			
	Total	Level 1	Level 2	Level 3
Cash equivalents:				
Money market funds	\$ 62,452	\$ 62,452	\$ —	\$ —
Total	<u>\$ 62,452</u>	<u>\$ 62,452</u>	<u>\$ —</u>	<u>\$ —</u>

There have been no transfers between fair value levels during the three months ended March 31, 2018 or 2019.

4. Property and Equipment, Net

Property and equipment, net consisted of the following (in thousands):

	December 31, 2018	March 31, 2019
Lab equipment	\$ 4,847	\$ 5,305
Furniture and fixtures	542	542
Computer equipment	517	512
Software	90	90
Leasehold improvements	6,174	6,174
Construction in process	334	—
Total property and equipment	12,504	12,623
Less: accumulated depreciation	(1,958)	(2,398)
Property and equipment, net	<u>\$ 10,546</u>	<u>\$ 10,225</u>

Depreciation expense for the three months ended March 31, 2018 and 2019 was \$0.2 million and \$0.5 million, respectively.

Fulcrum Therapeutics, Inc.**Notes to Consolidated Financial Statements (Continued)****5. Additional Balance Sheet Detail**

Prepaid expenses and other current assets consisted of the following (in thousands):

	December 31, 2018	March 31, 2019
Prepaid expenses	\$ 460	\$ 508
Prepaid sign-on bonuses subject to vesting provisions	99	229
Leasehold improvement allowance receivable	366	366
Interest income receivable	135	123
Other	238	318
Total prepaid expenses and other current assets	<u>\$ 1,298</u>	<u>\$ 1,544</u>

Accrued expenses and other current liabilities consisted of the following (in thousands):

	December 31, 2018	March 31, 2019
External research and development	\$ 437	\$ 889
Payroll and benefits	1,448	527
Professional services	254	170
Capital lease obligation, current portion	46	47
Restricted stock liability, current portion	18	15
Property and equipment purchases	174	—
Other	120	51
Total accrued expenses and other current liabilities	<u>\$ 2,497</u>	<u>\$ 1,699</u>

6. Convertible Preferred Stock

As of December 31, 2018, 100,000,000 shares of convertible preferred stock were authorized, issued, and outstanding, of which 60,000,000 shares were designated as \$0.001 par value Series A convertible preferred stock (the "Series A Preferred Stock"), and 40,000,000 shares were designated as \$0.001 par value Series B convertible preferred stock (the "Series B Preferred Stock", and together with the Series A Preferred Stock, the "Preferred Stock"). As of March 31, 2019, 112,500,000 shares of Preferred Stock were authorized, issued, and outstanding, of which 60,000,000 shares were designated as \$0.001 par value Series A Preferred Stock, and 52,500,000 shares were designated as \$0.001 par value Series B Preferred Stock.

During the three months ended March 31, 2019, the Company issued 12,500,000 shares of Series B Preferred Stock in connection with the GSK Agreement (Note 9). The rights, privileges, and preferences of the Series B Preferred Stock issued in connection with the GSK Agreement are consistent with the rights, privileges, and preferences of the Series B Preferred Stock issued during the year ended December 31, 2018.

No dividends have been declared since inception. Aggregate cumulative dividends associated with the Series A Preferred Stock and the Series B Preferred Stock as of December 31, 2018 were \$7.2 million and \$2.3 million, respectively. Aggregate cumulative dividends associated with the Series A Preferred Stock and the Series B Preferred Stock as of March 31, 2019 were \$8.4 million and \$4.1 million, respectively.

Fulcrum Therapeutics, Inc.**Notes to Consolidated Financial Statements (Continued)****7. Common Stock**

Common stockholders are entitled to receive dividends, as may be declared by the Company's board of directors, if any, subject to the preferential dividend rights of the Preferred Stock. No dividends have been declared or paid during the three months ended March 31, 2018 or 2019.

During the three months ended March 31, 2019, the Company's Certificate of Incorporation was amended and restated to increase the number of authorized shares of Common Stock from 135,000,000 to 147,500,000 shares.

The Company had reserved the following shares of Common Stock for the potential conversion of Preferred Stock and for the future issuance of Common Stock pursuant to the Company's 2016 Stock Incentive Plan, as amended from time to time (the "2016 Plan"):

	<u>December 31,</u> <u>2018</u>	<u>March 31,</u> <u>2019</u>
Shares reserved for conversion of outstanding Series A Preferred Stock	60,000,000	60,000,000
Shares reserved for conversion of outstanding Series B Preferred Stock	40,000,000	52,500,000
Shares reserved for future issuance under the 2016 Stock Incentive Plan	6,432,941	2,565,912
	<u>106,432,941</u>	<u>115,065,912</u>

8. Stock-based Compensation Expense***Grants Under the 2016 Stock Incentive Plan***

In July 2016, the Company adopted the 2016 Plan, under which it may grant restricted stock awards, restricted stock units, incentive stock options, non-statutory stock options, and other stock-based awards to eligible employees, officers, directors, consultants, and advisors. The total number of shares of Common Stock that were authorized for issuance under the 2016 Plan was 22,465,000 as of December 31, 2018. In January 2019, the 2016 Plan was amended to increase the number of shares of Common Stock reserved for issuance under the 2016 Plan by 2,500,000 shares. The total number of shares of Common Stock that were authorized for issuance under the 2016 Plan was 24,965,000 as of March 31, 2019.

For financial reporting purposes, the Company performed Common Stock valuations with the assistance of a third-party specialist as of March 15, 2019, November 30, 2018, August 24, 2018, June 1, 2018, December 31, 2017, and December 31, 2016 to determine stock-based compensation expense for restricted stock awards and stock options.

Shares of Common Stock repurchased from employees and non-employees are shares held in the Company's treasury ("Treasury Shares"). The board of directors may, at its discretion, authorize that the Treasury Shares be returned to the pool of authorized but unissued Common Stock.

Fulcrum Therapeutics, Inc.**Notes to Consolidated Financial Statements (Continued)****8. Stock-based Compensation Expense (Continued)**

The following table summarizes the Company's restricted stock activity under the 2016 Plan since December 31, 2018:

	Number of Shares	Weighted Average Grant Date Fair Value
Unvested at December 31, 2018	5,299,003	\$ 0.44
Granted	—	—
Vested	(741,900)	0.43
Repurchased	(307,463)	0.44
Unvested at March 31, 2019	<u>4,249,640</u>	<u>\$ 0.44</u>

The following table summarizes the Company's stock option activity under the 2016 Plan since December 31, 2018:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value
Outstanding at December 31, 2018	3,555,302	\$ 1.02	9.84	\$ 367,427
Granted	7,143,661	1.12		
Exercised	—	—		
Cancelled	—	—		
Outstanding at March 31, 2019	<u>10,698,963</u>	\$ 1.09	9.74	\$ 1,109,354
Exercisable at March 31, 2019	<u>522,930</u>	\$ 0.97	9.62	\$ 113,092

The aggregate intrinsic value of stock options is calculated as the difference between the exercise price of the stock options and the fair value of the Company's Common Stock as of the balance sheet date for those options that had exercise prices lower than the fair value of the Company's Common Stock.

The weighted average grant date fair value of stock options granted during the three months ended March 31, 2019 was \$0.79 per share. As of March 31, 2019, no stock options have been exercised since inception. The fair value of stock options granted during the three months ended March 31, 2019 under the 2016 Plan has been calculated on the date of grant using the following weighted average assumptions:

	Three Months Ended March 31, 2019
Risk-free interest rate	2.6%
Expected dividend yield	0.0%
Expected term (years)	6.0
Expected stock price volatility	81.4%

Fulcrum Therapeutics, Inc.**Notes to Consolidated Financial Statements (Continued)****8. Stock-based Compensation Expense (Continued)****Grants Outside the 2016 Stock Incentive Plan**

The following table summarizes the Company's restricted stock activity outside of the 2016 Plan since December 31, 2018:

	Number of Shares	Weighted Average Grant Date Fair Value
Unvested at December 31, 2018	3,127,500	\$ 0.42
Granted	—	—
Vested	(196,250)	0.42
Repurchased	—	—
Unvested at March 31, 2019	<u>2,931,250</u>	<u>\$ 0.42</u>

The aggregate intrinsic value of all restricted stock awards that vested during the three months ended March 31, 2019 was \$1.4 million.

Stock-based Compensation Expense

The total compensation cost recognized in the statements of operations associated with all stock-based compensation awards granted by the Company is as follows (in thousands):

	Three Months Ended March 31, 2018	Three Months Ended March 31, 2019
Research and development	\$ 256	\$ 406
General and administrative	173	415
Total stock-based compensation expense	<u>\$ 429</u>	<u>\$ 821</u>

As of March 31, 2019, the Company had an aggregate of \$10.5 million of unrecognized stock-based compensation expense, which is expected to be recognized over a weighted average period of 3.26 years.

9. Asset Acquisition

In February 2019, the Company entered into a right of reference and license agreement (the "GSK Agreement") with subsidiaries of GlaxoSmithKline plc (collectively referred to as "GSK"), pursuant to which the Company has been granted an exclusive worldwide license to develop and commercialize losmapimod. Under the GSK Agreement, the Company also acquired reference rights to relevant regulatory and manufacturing documents and GSK's existing supply of losmapimod drug substance and product. The Company also has the right to sublicense its rights under the license agreement, subject to certain conditions. The Company is obligated to use commercially reasonable efforts to develop and commercialize losmapimod at its sole cost. The Company is also responsible for costs related to the filing and maintenance of the licensed patent rights.

Under the GSK Agreement, the Company issued 12,500,000 million shares of Series B Preferred Stock to GSK with an estimated fair value of \$25.5 million, or \$2.04 per share, which was determined with the assistance of a third-party specialist contemporaneously with the issuance of the Series B Preferred Stock to GSK. In addition, the Company may owe GSK up to \$37.5 million in certain specified clinical and

Fulcrum Therapeutics, Inc.**Notes to Consolidated Financial Statements (Continued)****9. Asset Acquisition (Continued)**

regulatory milestones, of which \$2.5 million is due upon the initiation of a Phase 2 clinical trial, and up to \$60.0 million in certain specified sales milestones. The Company has agreed to pay tiered royalties on annual net sales of losmapimod that range from mid single-digit percentages to a low double-digit, but less than teens, percentage. The royalties are payable on a product-by-product and country-by-country basis, and may be reduced in specified circumstances. The Company also incurred \$0.1 million of direct expenses related to the transaction, which the Company included in the total consideration for the transaction.

The GSK Agreement may be terminated by either party for a material breach by the other, subject to notice and cure provisions. Unless earlier terminated, the GSK Agreement will continue in effect until the expiration of the Company's royalty obligations, which expire on a country-by-country basis on the later of (i) ten years after the first commercial sale in the country or (ii) approval of a generic version of losmapimod by the applicable regulatory agency.

The Company concluded the arrangement did not result in the acquisition of a business, as substantially all of the fair value of the gross assets acquired was concentrated in a single in-process research and development asset, losmapimod. In addition, the Company did not obtain any substantive processes in connection to the GSK Agreement and losmapimod was not generating revenue at the time the GSK Agreement was executed. Therefore, the Company accounted for the arrangement as an asset acquisition. The Company also concluded that the acquired assets do not have an alternative future use, and therefore the fair value attributable to the GSK Agreement of \$25.6 million, inclusive of transaction costs, was recorded as in-process research and development expense (a component of research and development expenses) in the Company's consolidated statement of operations and comprehensive loss for the three months ended March 31, 2019, which is the period in which the Company obtained (i) the license to losmapimod, (ii) the right to reference relevant regulatory and manufacturing documents, and (iii) GSK's existing supply of losmapimod drug substance and product. Additionally, the Company will recognize clinical and regulatory milestone payments when the underlying contingency is resolved and the consideration is paid or becomes payable. The milestone payments will be capitalized or expensed depending on the nature of the associated asset as of the date of recognition. The Company will record sales milestone payments and royalties as additional expense of the related product sales in the period in which the corresponding sales occur.

10. Commitments and Contingencies***Operating Leases***

In May 2016, the Company entered into a sublease agreement for approximately 8,143 square feet of office and laboratory space at its prior corporate headquarters in Cambridge, Massachusetts. The sublease for this space terminated on June 30, 2018. Rent expense associated with this sublease for the three months ended March 31, 2018 was \$0.1 million.

In November 2017, the Company entered into a lease agreement for its current corporate headquarters for approximately 28,731 square feet of office and laboratory space in Cambridge, Massachusetts. The lease has a total commitment of \$25.1 million over the ten year term, and includes escalating rent payments. The lease agreement requires the Company to either pay a security deposit or maintain a letter of credit of \$1.1 million. The Company maintains a letter of credit for this lease and has recorded the cash held to secure the letter of credit as restricted cash on the consolidated balance sheet as of December 31, 2018 and March 31, 2019. Rent expense associated with this lease for the three months ended March 31, 2018 and 2019 was approximately \$0.5 million and \$0.5 million, respectively.

Fulcrum Therapeutics, Inc.**Notes to Consolidated Financial Statements (Continued)****10. Commitments and Contingencies (Continued)**

The future minimum lease payments associated with the lease for the Company's current headquarters as of March 31, 2019, are as follows (in thousands):

2019 ⁽¹⁾	\$ 1,673
2020	2,285
2021	2,354
2022	2,424
2023	2,497
Thereafter	12,187
Total minimum lease payments	<u>\$ 23,420</u>

(1) Amounts are for the nine months ending December 31, 2019.

Other Agreements

The Company has agreements with third parties in the normal course of business under which it can license certain developed technologies. If the Company exercises its rights to license the technologies it may be subject to additional fees and milestone payments. As of March 31, 2019, the Company has not exercised its rights to license such technologies.

Indemnification Agreements

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, business partners and other parties with respect to certain matters arising out of the relationship between such parties and the Company. In addition, the Company has entered into indemnification agreements with members of its board of directors and senior management that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is, in many cases, unlimited. To date, the Company has not incurred any material costs as a result of such indemnifications. The Company is not aware of any claims under indemnification arrangements, and it has not accrued any liabilities related to such obligations as of December 31, 2018 or March 31, 2019.

Legal Proceedings

The Company is not currently a party to any material legal proceedings. At each reporting date, the Company evaluates whether or not a potential loss amount or a potential range of loss is probable and reasonably estimable under the provisions of the authoritative guidance that addresses accounting for contingencies. The Company expenses the costs related to its legal proceedings as they are incurred. No such costs have been incurred during the three months ended March 31, 2018 or 2019.

11. Defined Contribution Plan

The Company has a defined contribution savings plan under Section 401(k) of the Internal Revenue Code (the "401(k) Plan"). The 401(k) Plan covers all employees who meet defined minimum age and service requirements, and allows participants the option to elect to defer a portion of their annual

Fulcrum Therapeutics, Inc.**Notes to Consolidated Financial Statements (Continued)****11. Defined Contribution Plan (Continued)**

compensation on a pretax basis. As currently established, the Company is not required to make and has not made any contributions to the 401(k) Plan.

12. Net Loss per Share and Pro Forma Net Loss per Share***Net Loss per Share***

The following common stock equivalents were excluded from the calculation of diluted net loss per share attributable to common stockholders for the periods indicated because including them would have had an anti-dilutive effect:

	Three Months Ended March 31, 2018	Three Months Ended March 31, 2019
Series A Preferred Stock	47,333,333	60,000,000
Series B Preferred Stock	—	52,500,000
Outstanding stock options	—	10,698,963
Unvested restricted stock awards	12,381,253	7,180,890
Total	59,714,586	130,379,853

Pro Forma Net Loss per Share

The pro forma basic and diluted net loss per share attributable to common stockholders for the three months ended March 31, 2019 give effect to adjustments arising upon the closing of a qualified IPO. The pro forma basic and diluted weighted average common shares outstanding used in the calculation of pro forma basic and diluted net loss per share attributable to common stockholders for the three months ended March 31, 2019 give effect to the automatic conversion upon a qualified IPO of all outstanding shares of Preferred Stock into shares of Common Stock as if the conversion had occurred on the later of January 1, 2019 or the issuance date of the Preferred Stock. Accordingly, the pro forma basic and diluted net loss per share attributable to stockholders does not include the effects of the cumulative preferred stock dividends. Shares to be sold in the offering are excluded from the pro forma basic and diluted loss per share attributable to common stockholders calculations.

Fulcrum Therapeutics, Inc.**Notes to Consolidated Financial Statements (Continued)****12. Net Loss per Share and Pro Forma Net Loss per Share (Continued)**

The following table summarizes the Company's pro forma net loss per share attributable to common stockholders (in thousands, except per share data):

	<u>Three Months Ended</u> <u>March 31, 2019</u>
Numerator:	
Net loss attributable to common stockholders	\$ (39,884)
Cumulative convertible preferred stock dividends	3,041
Pro forma net loss attributable to common stockholders	<u>\$ (36,843)</u>
Denominator:	
Weighted average common shares outstanding	11,497
Pro forma weighted average shares outstanding after giving effect to the conversion of Preferred Stock	107,083
Pro forma weighted average shares outstanding	<u>118,580</u>
Pro forma basic and diluted loss per share attributable to common stockholders, basic and diluted	<u>\$ (0.31)</u>

13. Related-Party Transactions

During the three months ended March 31, 2018 and 2019, the Company paid fees to Third Rock Ventures, LLC ("TRV"), an affiliate of one of the Company's principal stockholders, in exchange for consulting services. The Company recorded expenses related to such fees of less than \$0.1 million during each of the three months ended March 31, 2018 and 2019. As of both December 31, 2018 and March 31, 2019, there was less than \$0.1 million of amounts due to TRV for such services that were included in accounts payable and accrued expenses. Additionally, consultants that provide services to the Company are employees of TRV. The Company has issued an aggregate of 996,000 shares of Common Stock to these consultants in exchange for their continuing consulting services.

During the three months ended March 31, 2018, the Company recorded other income of \$0.4 million related to the sale of drug material to an entity affiliated with TRV.

14. Subsequent Events

For its consolidated financial statements as of March 31, 2019 and for the three months then ended, the Company evaluated subsequent events through June 5, 2019, the date on which those consolidated financial statements were issued.

Shares



Common Stock

Prospectus

MORGAN STANLEY

BofA MERRILL LYNCH

SVB LEERINK

, 2019

Until _____, 2019 (25 days after the date of this prospectus), all dealers that effect transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This delivery requirement is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

PART II
INFORMATION NOT REQUIRED IN PROSPECTUS

Item 13. Other Expenses of Issuance and Distribution.

The following table sets forth the expenses to be incurred in connection with the offering described in this Registration Statement, other than underwriting discounts and commissions, all of which will be paid by the Registrant. All amounts are estimates except the Securities and Exchange Commission, or SEC, registration fee, the Financial Industry Regulatory Authority, Inc. filing fee and the Nasdaq Global Market initial listing fee.

	<u>Amount</u>
Securities and Exchange Commission registration fee	\$ 10,453.50
Financial Industry Regulatory Authority, Inc. filing fee	13,437.50
Nasdaq Global Market initial listing fee	*
Accountants' fees and expenses	*
Legal fees and expenses	*
Transfer agent's fees and expenses	*
Printing and engraving expenses	*
Miscellaneous	*
Total expenses	\$ *

* To be filed by amendment.

Item 14. Indemnification of Directors and Officers.

Section 102 of the Delaware General Corporation Law, or the DGCL, permits a corporation to eliminate the personal liability of its directors or its stockholders for monetary damages for a breach of fiduciary duty as a director, except where the director breached his or her duty of loyalty, failed to act in good faith, engaged in intentional misconduct or knowingly violated a law, authorized the payment of a dividend or approved a stock repurchase in violation of Delaware corporate law or obtained an improper personal benefit. Our certificate of incorporation that will be effective upon the closing of this offering provides that no director shall be personally liable to us or our stockholders for monetary damages for any breach of fiduciary duty as a director, notwithstanding any provision of law imposing such liability, except to the extent that the DGCL prohibits the elimination or limitation of liability of directors for breaches of fiduciary duty.

Section 145 of the DGCL provides that a corporation has the power to indemnify a director, officer, employee or agent of the corporation and certain other persons serving at the request of the corporation in related capacities against expenses (including attorneys' fees), judgments, fines and amounts paid in settlements actually and reasonably incurred by the person in connection with an action, suit or proceeding to which he or she is or is threatened to be made a party by reason of such position, if such person acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the corporation, and, in any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful, except that, in the case of actions brought by or in the right of the corporation, no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or other adjudicating court determines that, despite the adjudication of liability but in view of all of the circumstances of the case, such person is fairly and reasonably entitled to indemnification for such expenses which the Court of Chancery or such other court shall deem proper.

Our certificate of incorporation that will be effective upon the closing of the offering provides that we will indemnify each person who was or is a party or threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of us), by reason of the fact that he or she is or was, or has agreed to become, our director or officer, or is or was serving, or has agreed to serve, at our request as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (all such persons being referred to as an Indemnitee), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding and any appeal therefrom if such Indemnitee acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, our best interests, and, with respect to any criminal action or proceeding, he or she had no reasonable cause to believe his or her conduct was unlawful.

Our certificate of incorporation that will be effective upon the closing of the offering also provides that we will indemnify any Indemnitee who was or is a party to an action or suit by or in the right of us to procure a judgment in our favor by reason of the fact that the Indemnitee is or was, or has agreed to become, our director or officer, or is or was serving, or has agreed to serve, at our request as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise, or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees) and, to the extent permitted by law, amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding, and any appeal therefrom, if the Indemnitee acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, our best interests, except that no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to us, unless a court determines that, despite such adjudication but in view of all of the circumstances, he or she is entitled to indemnification of such expenses. Notwithstanding the foregoing, to the extent that any Indemnitee has been successful, on the merits or otherwise, he or she will be indemnified by us against all expenses (including attorneys' fees) actually and reasonably incurred by him or her or on his or her behalf in connection therewith. If we do not assume the defense, expenses must be advanced to an Indemnitee under certain circumstances.

In addition, we intend to enter into indemnification agreements with all of our executive officers and directors prior to the completion of this offering. In general, these agreements provide that we will indemnify the executive officer or director to the fullest extent permitted by law for claims arising in his or her capacity as an executive officer or director of our company or in connection with his or her service at our request for another corporation or entity. The indemnification agreements also provide for procedures that will apply in the event that an executive officer or director makes a claim for indemnification and establish certain presumptions that are favorable to the executive officer or director.

We maintain a general liability insurance policy that covers certain liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers.

The underwriting agreement we will enter into in connection with the offering of common stock being registered hereby provides that the underwriters will indemnify, under certain conditions, our directors and officers (as well as certain other persons) against certain liabilities arising in connection with such offering.

Insofar as the foregoing provisions permit indemnification of directors, executive officers or persons controlling us for liability arising under the Securities Act of 1933, as amended, or the Securities Act, we have been informed that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

Item 15. Recent Sales of Unregistered Securities.

Set forth below is information regarding shares of our common stock, shares of our preferred stock and stock options granted by us within the past three years that were not registered under the Securities Act. Also included is the consideration, if any, received by us for such shares and options and information relating to the section of the Securities Act, or rule of the SEC, under which exemption from registration was claimed.

(a) Issuances of Preferred Stock and Convertible Promissory Notes

On April 14, 2016, we issued and sold a convertible promissory note to one investor in the aggregate principal amount of \$3,500,000. The note accrued interest at a rate of 6% per annum. On July 18, 2016, all principal and accrued but unpaid interest under the note was converted into shares of Series A preferred stock, at a price per share of \$1.00.

On July 18, 2016, we issued and sold 11,843,493 shares of our Series A preferred stock to one investor, consisting of (i) 5,156,507 shares sold for cash at a price per share of \$1.00, for an aggregate purchase price of \$5,156,507 and (ii) 6,686,986 shares issued upon conversion of \$6,686,986 in outstanding principal and accrued but unpaid interest under our convertible promissory notes issued on October 15, 2015 and April 14, 2016, at a price per share of \$1.00.

On November 15, 2016, we issued and sold 5,156,507 shares of our Series A preferred stock to one investor at a price per share of \$1.00 in cash, for an aggregate purchase price of \$5,156,507.

On February 17, 2017, we issued and sold 6,333,333 shares of our Series A preferred stock to one investor at a price per share of \$1.00 in cash, for an aggregate purchase price of \$6,333,333.

On April 28, 2017, we issued and sold 5,000,000 shares of our Series A preferred stock to one investor at a price per share of \$1.00 in cash, for an aggregate purchase price of \$5,000,000.

On May 3, 2017, we issued and sold 6,333,333 shares of our Series A preferred stock to two investors at a price per share of \$1.00 in cash, for an aggregate purchase price of \$6,333,333.

On January 4, 2018, we issued and sold 6,333,334 shares of our Series A preferred stock to two investors at a price per share of \$1.00 in cash, for an aggregate purchase price of \$6,333,334.

On March 13, 2018, we issued and sold 6,333,333 shares of our Series A preferred stock to two investors at a price per share of \$1.00 in cash, for an aggregate purchase price of \$6,333,333.

On May 9, 2018, we issued and sold 6,333,333 shares of our Series A preferred stock to two investors at a price per share of \$1.00 in cash, for an aggregate purchase price of \$6,333,333.

On June 6, 2018, we issued and sold 6,333,334 shares of our Series A preferred stock to two investors at a price per share of \$1.00 in cash, for an aggregate purchase price of \$6,333,334.

On August 24, 2018, we issued and sold 40,000,000 shares of our Series B preferred stock to 20 investors at a price per share of \$2.00 in cash, for an aggregate purchase price of \$80,000,000.

On February 8, 2019 we issued 12,500,000 shares of our Series B preferred stock to one investor in exchange for a license.

No underwriters were involved in the foregoing issuances of securities. The securities described in this section (a) of Item 15 were issued to investors in reliance upon the exemption from the registration requirements of the Securities Act, as set forth in Section 4(a)(2) under the Securities Act and, in certain cases, Regulation D thereunder, relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required. All purchasers received written disclosures that the securities had not been registered under the Securities Act and that any resale must be made pursuant to a registration statement or an available exemption from such registration.

(b) Restricted Common Stock

Between June 21, 2016 and June 21, 2019, we issued an aggregate of 18,254,818 shares of restricted common stock, for cash with purchase prices ranging from \$0.001 to \$0.01 per share, to employees, directors, advisors and consultants, including 12,719,818 shares issued pursuant to our 2016 Stock Incentive Plan, as amended.

The shares of common stock described in this section (b) of Item 15 were issued pursuant to written compensatory plans or arrangements with our employees, directors, advisors and consultants, in reliance on the exemption provided by Rule 701 promulgated under the Securities Act, or pursuant to Section 4(a)(2) under the Securities Act, relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required. All recipients either received adequate information about our company or had access, through employment or other relationships, to such information.

(c) Stock Option Grants and Exercises

Between June 21, 2016 and June 21, 2019, we granted options to purchase an aggregate of 11,356,963 shares of common stock, with exercise prices ranging from \$0.69 to \$1.58 per share, to our employees, directors, advisors and consultants pursuant to our 2016 Stock Incentive Plan. Between June 21, 2016 and June 21, 2019, we issued 197,448 shares of our common stock upon the exercise of stock options outstanding under our 2016 Stock Incentive Plan for aggregate consideration of \$220,315.

The stock options and the shares of common stock issued upon the exercise of stock options described in this section (c) of Item 15 were issued pursuant to written compensatory plans or arrangements with our employees, directors, advisors and consultants, in reliance on the exemption provided by Rule 701 promulgated under the Securities Act, or pursuant to Section 4(a)(2) under the Securities Act, relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required. All recipients either received adequate information about our company or had access, through employment or other relationships, to such information.

Item 16. Exhibits and Financial Statement Schedules.

(a) **Exhibits**

<u>Exhibit Number</u>	<u>Description of Exhibit</u>
1.1	Form of Underwriting Agreement
3.1	Amended and Restated Certificate of Incorporation, as amended, of the Registrant
3.2	Bylaws of the Registrant
3.3	Form of Restated Certificate of Incorporation of the Registrant (to be effective upon the closing of this offering)
3.4	Form of Amended and Restated Bylaws of the Registrant (to be effective upon the closing of this offering)
4.1	Specimen Stock Certificate evidencing the shares of common stock
5.1*	Opinion of Wilmer Cutler Pickering Hale and Dorr LLP
10.1	Amended and Restated Investors' Rights Agreement, dated as of August 24, 2018, by and among the Registrant and the other parties thereto
10.2	2016 Stock Incentive Plan, as amended
10.3	Form of Incentive Stock Option Agreement under the 2016 Stock Incentive Plan
10.4	Form of Non-Statutory Stock Option Agreement under the 2016 Stock Incentive Plan
10.5	Form of Restricted Stock Agreement under the 2016 Stock Incentive Plan
10.6*	2019 Stock Incentive Plan
10.7*	Form of Stock Option Agreement under the 2019 Stock Incentive Plan
10.8*	2019 Employee Stock Purchase Plan
10.9*	Summary of Non-Employee Director Compensation Program
10.10 †	Right of Reference and License Agreement, dated as of February 8, 2019, by and among the Registrant, GlaxoSmithKline Intellectual Property (No. 2) Limited, GlaxoSmithKline LLC and Glaxo Group Limited
10.11	Lease for 26 Landsdowne Street, dated November 22, 2017, by and between the UP 26 Landsdowne, LLC and the Registrant
10.12	Offer of Employment, dated June 13, 2016, by and between the Registrant and Robert Gould
10.13	Offer of Employment, dated December 6, 2018, by and between the Registrant and Bryan Stuart
10.14	Offer of Employment, dated August 10, 2016, by and between the Registrant and Diego Cadavid
10.15	Form of Indemnification Agreement between the Registrant and each of its Executive Officers and Directors
21.1	Subsidiary of the Registrant
23.1	Consent of Ernst & Young LLP, independent registered public accounting firm
23.2*	Consent of Wilmer Cutler Pickering Hale and Dorr LLP (included in Exhibit 5.1)
24.1	Power of Attorney (included on signature page)

* To be filed by amendment.

† Certain portions of this exhibit have been omitted because they are not material and would likely cause competitive harm to the Registrant if disclosed.

(b) **Financial Statement Schedules**

No financial statement schedules are provided because the information called for is not required or is shown either in the financial statements or the related notes.

Item 17. Undertakings.

(a) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

(b) The undersigned registrant hereby undertakes that:

- (1) For purposes of determining any liability under the Securities Act of 1933, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.
- (2) For the purpose of determining any liability under the Securities Act of 1933, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ ALAN EZEKOWITZ</u> Alan Ezekowitz, MBChB, D. Phil	Director	June 21, 2019
<u>/s/ JAMES GERAGHTY</u> James Geraghty	Director	June 21, 2019
<u>/s/ KATE HAVILAND</u> Kate Haviland	Director	June 21, 2019

[·] Shares

FULCRUM THERAPEUTICS, INC.

COMMON STOCK, PAR VALUE \$0.001 PER SHARE

UNDERWRITING AGREEMENT

[·], 2019

Morgan Stanley & Co. LLC
BofA Securities, Inc.
SVB Leerink LLC

c/o Morgan Stanley & Co. LLC
1585 Broadway
New York, New York 10036

c/o BofA Securities, Inc.
One Bryant Park
New York, New York 10036

c/o SVB Leerink LLC
One Federal Street, 37th Floor
Boston, Massachusetts 02110

Ladies and Gentlemen:

Fulcrum Therapeutics, Inc., a Delaware corporation (the “**Company**”), proposes to issue and sell to the several Underwriters named in Schedule I hereto (the “**Underwriters**”), for whom Morgan Stanley & Co. LLC, BofA Securities, Inc. and SVB Leerink LLC are acting as representatives (the “**Representatives**”), [•] shares of its common stock, par value \$0.001 per share (the “**Firm Shares**”). The Company also proposes to issue and sell to the several Underwriters not more than an additional [•] shares of its common stock, par value \$0.001 per share (the “**Additional Shares**”), if and to the extent that the Representatives shall have determined to exercise, on behalf of the Underwriters, the right to purchase such shares of common stock granted to the Underwriters in Section 2 hereof. The Firm Shares and the Additional Shares are hereinafter collectively referred to as the “**Shares**.” The shares of common stock, par value \$0.001 per share, of the Company to be outstanding after giving effect to the sales contemplated hereby are hereinafter referred to as the “**Common Stock**.”

The Company has filed with the Securities and Exchange Commission (the “**Commission**”) a registration statement on Form S-1, including a prospectus, relating to the Shares. The registration statement as amended at the time it becomes effective, including the information (if any) deemed to be part of the registration statement at the time of effectiveness pursuant to Rule 430A under the Securities Act of 1933, as amended (the “**Securities Act**”), is hereinafter referred to as the “**Registration Statement**”; the prospectus in the form first used to confirm sales of Shares (or in the form first made available to the Underwriters by the Company to meet requests of purchasers pursuant to Rule 173 under the Securities Act) is hereinafter referred to as the “**Prospectus**.” If the Company has filed an abbreviated registration statement to register additional shares of Common Stock pursuant to Rule 462(b) under the Securities Act (a

“**Rule 462 Registration Statement**”), then any reference herein to the term “**Registration Statement**” shall be deemed to include such Rule 462 Registration Statement.

For purposes of this Agreement, “**free writing prospectus**” has the meaning set forth in Rule 405 under the Securities Act, “**Time of Sale Prospectus**” means the preliminary prospectus contained in the Registration Statement at the time of its effectiveness together with the documents and pricing information set forth in Schedule II hereto, and “**broadly available road show**” means a “bona fide electronic road show” as defined in Rule 433(h) (5) under the Securities Act that has been made available without restriction to any person. As used herein, the terms “Registration Statement,” “preliminary prospectus,” “Time of Sale Prospectus” and “Prospectus” shall include the documents, if any, incorporated by reference therein as of the date hereof.

1. *Representations and Warranties.* The Company represents and warrants to and agrees with each of the Underwriters that:

(a) The Registration Statement has become effective; no stop order suspending the effectiveness of the Registration Statement is in effect, and no proceedings for such purpose or pursuant to Section 8A under the Securities Act are pending before or, to the Company’s knowledge, threatened by the Commission.

(b) (i) The Registration Statement, when it became effective, did not contain and, as amended or supplemented, if applicable, will not contain any untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein not misleading, (ii) the Registration Statement and the Prospectus comply and, as amended or supplemented, if applicable, will comply in all material respects with the Securities Act and the applicable rules and regulations of the Commission thereunder, (iii) the Time of Sale Prospectus does not, and at the time of each sale of the Shares in connection with the offering when the Prospectus is not yet available to prospective purchasers and at the Closing Date (as defined in Section 4), the Time of Sale Prospectus, as then amended or supplemented by the Company, if applicable, will not, contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading, (iv) each broadly available road show, if any, when considered together with the Time of Sale Prospectus, does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading and (v) the Prospectus does not contain and, as amended or supplemented, if applicable, will not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading, except that the representations and warranties set forth in this paragraph do not apply to statements or omissions in the Registration Statement, the Time of Sale Prospectus or the Prospectus based

upon information relating to any Underwriter furnished to the Company in writing by such Underwriter through the Representatives expressly for use therein, it being understood and agreed upon that the only such information furnished by any Underwriter consists of the following information in the Prospectus furnished on behalf of each Underwriter: the concession and reallowance figures appearing the third paragraph under the caption “Underwriters” and the information contained in the thirteenth paragraph under the caption “Underwriters”.

(c) The Company is not an “ineligible issuer” in connection with the offering pursuant to Rules 164, 405 and 433 under the Securities Act. Any free writing prospectus that the Company is required to file pursuant to Rule 433(d) under the Securities Act has been, or will be, filed with the Commission in accordance with the requirements of the Securities Act and the applicable rules and regulations of the Commission thereunder. Each free writing prospectus that the Company has filed, or is required to file, pursuant to Rule 433(d) under the Securities Act or that was prepared by or on behalf of or used or referred to by the Company complies or will comply in all material respects with the requirements of the Securities Act and the applicable rules and regulations of the Commission thereunder. Except for the free writing prospectuses, if any, identified in Schedule II hereto, and electronic road shows, if any, each furnished to the Representatives before first use, the Company has not prepared, used or referred to, and will not, without the prior consent of each of the Representatives, prepare, use or refer to, any free writing prospectus.

(d) The Company has been duly incorporated, is validly existing as a corporation in good standing under the laws of the State of Delaware, has the corporate power and authority to own its property and to conduct its business as described in the Time of Sale Prospectus and is duly qualified to transact business and is in good standing in each jurisdiction in which the conduct of its business or its ownership or leasing of property requires such qualification, except to the extent that the failure to be so qualified or be in good standing would not have a material adverse effect on the Company and its Subsidiary (as defined in Section 1(e)), taken as a whole.

(e) Fulcrum Therapeutics Securities Corp. (the “**Subsidiary**”) is the only subsidiary of the Company. The Subsidiary has been duly incorporated, is validly existing as a corporation in good standing under the laws of the Commonwealth of Massachusetts, has the corporate power and authority to own its property and to conduct its business as described in the Time of Sale Prospectus and is duly qualified to transact business and is in good standing in each jurisdiction in which the conduct of its business or its ownership or leasing of property requires such qualification, except to the extent that the failure to be so qualified or be in good standing would not reasonably be expected to have a material adverse effect on the Company and its Subsidiary, taken as a whole; all of the issued shares of capital stock of the Subsidiary have been duly and validly authorized and issued, are fully paid and non-assessable and are owned directly by the Company, free and clear of all liens, encumbrances, equities or claims.

(f) This Agreement has been duly authorized, executed and delivered by the Company.

(g) The authorized capital stock of the Company conforms in all material respects as to legal matters to the description thereof contained under the headings “Capitalization” and “Description of Capital Stock” in the Time of Sale Prospectus and the Prospectus.

(h) The shares of Common Stock outstanding prior to the issuance of the Shares have been duly authorized and are validly issued, fully paid and non-assessable.

(i) The Shares have been duly authorized and, when issued and delivered in accordance with the terms of this Agreement, will be validly issued, fully paid and non-assessable, and the issuance of such Shares will not be subject to any preemptive or similar rights that have not been validly waived.

(j) Neither the execution and delivery by the Company of, and the performance by the Company of its obligations under, this Agreement, nor the issuance and sale of the Shares, will (i) contravene any provision of applicable law, (ii) contravene any provision of the certificate of incorporation or by-laws of the Company, (iii) conflict with or result in a breach or violation of any of the terms or provisions of, or constitute a default under, any agreement or other instrument binding upon the Company or its Subsidiary that is material to the Company and its Subsidiary, taken as a whole, or (iv) result in any violation of any judgment, order or decree of any governmental body, agency or court having jurisdiction over the Company or its Subsidiary, except, in the case of clause (i) and (iii), as would not, individually or in the aggregate, reasonably be expected to have a material adverse effect on the Company and its Subsidiary, taken as a whole, or on the power and ability of the Company to perform its obligations under this Agreement. No consent, approval, authorization or order of, or qualification with, any governmental body or agency is required for the performance by the Company of its obligations under this Agreement, except such as have already been obtained or made or as may be required by the securities or Blue Sky laws of the various states or the rules and regulations of the Financial Industry Regulatory Authority (“**FINRA**”) or the or the Nasdaq Global Market in connection with the offer and sale of the Shares.

(k) There has not occurred any material adverse change, or any development that would reasonably be expected to result in a prospective material adverse change, in the condition, financial or otherwise, or in the earnings, business or operations of the Company and its Subsidiary, taken as a whole, from that set forth in the Time of Sale Prospectus.

(l) There are no legal or governmental proceedings pending or, to Company’s knowledge, threatened to which the Company or its Subsidiary is a party or to which any of the properties of the Company or its Subsidiary is subject

(i) other than proceedings described in the Time of Sale Prospectus and proceedings that, singly or in the aggregate, would not have a material adverse effect on the Company and its Subsidiary, taken as a whole, or on the power or ability of the Company to perform its obligations under this Agreement or to consummate the transactions contemplated by the Time of Sale Prospectus or (ii) that are required to be described in the Registration Statement or the Prospectus and are not so described; and there are no statutes, regulations, contracts or other documents that are required to be described in the Registration Statement or the Prospectus or to be filed as exhibits to the Registration Statement that are not described or filed as required.

(m) Each preliminary prospectus filed as part of the registration statement as originally filed or as part of any amendment thereto, or filed pursuant to Rule 424 under the Securities Act, complied when so filed in all material respects with the Securities Act and the applicable rules and regulations of the Commission thereunder.

(n) The Company is not, and after giving effect to the offering and sale of the Shares and the application of the proceeds thereof as described in the Prospectus will not be, required to register as an “investment company” as such term is defined in the Investment Company Act of 1940, as amended.

(o) The Company and its Subsidiary (i) are in compliance with any and all applicable foreign, federal, state and local laws and regulations relating to the protection of human health and safety, the environment or hazardous or toxic substances or wastes, pollutants or contaminants (“**Environmental Laws**”), (ii) have received all permits, licenses or other approvals required of them under applicable Environmental Laws to conduct their respective businesses and (iii) are in compliance with all terms and conditions of any such permit, license or approval, except where such noncompliance with Environmental Laws, failure to receive required permits, licenses or other approvals or failure to comply with the terms and conditions of such permits, licenses or approvals would not, singly or in the aggregate, reasonably be expected to have a material adverse effect on the Company and its Subsidiary, taken as a whole.

(p) There are no costs or liabilities associated with Environmental Laws (including, without limitation, any capital or operating expenditures required for clean-up, closure of properties or compliance with Environmental Laws or any permit, license or approval, any related constraints on operating activities and any potential liabilities to third parties) which would, singly or in the aggregate, reasonably be expected have a material adverse effect on the Company and its Subsidiary, taken as a whole.

(q) Except as described in the Time of Sale Prospectus and the Prospectus, there are no contracts, agreements or understandings between the Company and any person granting such person the right to require the Company to file a registration statement under the Securities Act with respect to any

securities of the Company or to require the Company to include such securities with the Shares registered pursuant to the Registration Statement; all such rights have been validly waived or complied with in connection with the issuance and sales of the Shares contemplated hereby.

(r) (i) None of the Company, the Subsidiary or the Company's controlled affiliates, or any director, officer or, to the Company's knowledge, any agent, representative or employee of the Company, the Subsidiary or the Company's controlled affiliates, has taken or will take any action in furtherance of an offer, payment, promise to pay, or authorization or approval of the payment, giving or receipt of money, property, gifts or anything else of value, directly or indirectly, to any government official (including any officer or employee of a government or government-owned or controlled entity or of a public international organization, or any person acting in an official capacity for or on behalf of any of the foregoing, or any political party or party official or candidate for political office) ("**Government Official**") in order to improperly influence official action, or to any person in violation of any applicable anti-corruption laws; (ii) the Company, the Subsidiary and the Company's controlled affiliates have conducted their businesses in compliance with applicable anti-corruption laws and have instituted and maintained and will continue to maintain policies and procedures reasonably designed to promote and achieve compliance with such laws and with the representations and warranties contained herein; and (iii) neither the Company nor its Subsidiary will use, directly or indirectly, the proceeds of the offering in furtherance of an offer, payment, promise to pay, or authorization of the payment or giving of money, or anything else of value, to any person in violation of any applicable anti-corruption laws.

(s) The operations of the Company and its Subsidiary are and have been conducted at all times, in all material respects, in compliance with all applicable financial recordkeeping and reporting requirements, including those of the Bank Secrecy Act, as amended by Title III of the Uniting and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism Act of 2001 (USA PATRIOT Act), and the applicable anti-money laundering statutes of jurisdictions where the Company or its Subsidiary conduct business, the rules and regulations thereunder and any related or similar rules, regulations or guidelines, issued, administered or enforced by any governmental agency having jurisdiction over the Company or its Subsidiary (collectively, the "**Anti-Money Laundering Laws**"), and no action, suit or proceeding by or before any court or governmental agency, authority or body or any arbitrator involving the Company or its Subsidiary with respect to the Anti-Money Laundering Laws is pending or, to the knowledge of the Company, threatened.

(t) (i) None of the Company, its Subsidiary, or any director, officer, or employee thereof, or, to the Company's knowledge, any agent, affiliate or representative of the Company or its Subsidiary, is an individual or entity ("**Person**") that is, or is owned or controlled by one or more Persons that are:

(A) the subject of any sanctions administered or enforced by the U.S. Department of Treasury's Office of Foreign Assets Control ("OFAC"), the United Nations Security Council ("UNSC"), the European Union ("EU"), Her Majesty's Treasury ("HMT"), or other relevant sanctions authority (collectively, "Sanctions"), or

(B) located, organized or resident in a country or territory that is the subject of Sanctions (including, without limitation, Crimea, Cuba, Iran, North Korea and Syria).

(ii) The Company will not, directly or indirectly, use the proceeds of the offering, or lend, contribute or otherwise make available such proceeds to any subsidiary, joint venture partner or other Person:

(A) to fund or facilitate any activities or business of or with any Person or in any country or territory that, at the time of such funding or facilitation, is the subject of Sanctions; or

(B) in any other manner that will result in a violation of Sanctions by any Person (including any Person participating in the offering, whether as underwriter, advisor, investor or otherwise).

(iii) The Company and its Subsidiary have not knowingly engaged in, are not now knowingly engaged in, and will not engage in, any dealings or transactions with any Person, or in any country or territory, that at the time of the dealing or transaction is or was the subject of Sanctions.

(u) Subsequent to the respective dates as of which information is given in each of the Registration Statement, the Time of Sale Prospectus and the Prospectus, (i) the Company and its Subsidiary have not incurred any material liability or obligation, direct or contingent, nor entered into any material transaction; (ii) the Company has not purchased any of its outstanding capital stock (other than from its employees or other service providers in connection with termination of such individuals' service to the Company pursuant to plans or agreements, as applicable), nor declared, paid or otherwise made any dividend or distribution of any kind on its capital stock other than ordinary and customary dividends; and (iii) there has not been any material change in the capital stock, short-term debt or long-term debt of the Company and its Subsidiary, except in each case as described in each of the Registration Statement, the Time of Sale Prospectus and the Prospectus, respectively.

(v) The Company and its Subsidiary do not own any real property and have good and marketable title to all personal property owned by them which is material to the business of the Company and its Subsidiary, in each case free and

clear of all liens, encumbrances and defects except such as are described in the Time of Sale Prospectus or such as do not materially affect the value of such property and do not interfere in any material respect with the use made and proposed to be made of such property by the Company and its Subsidiary; and any real property and buildings held under lease by the Company and its Subsidiary are held by them, as applicable, under valid, subsisting and, to the Company's knowledge, enforceable leases with such exceptions as are not material and do not interfere in any material respect with the use made and proposed to be made of such property and buildings by the Company and its Subsidiary, in each case except as described in the Time of Sale Prospectus.

(w) (i) The Company and its Subsidiary own or have a valid license to all patents and patent applications, inventions, copyrights, know how (including trade secrets and other unpatented and/or unpatentable proprietary or confidential information, systems or procedures), trademarks, service marks and trade names (collectively, "**Intellectual Property Rights**") used in or reasonably necessary to the conduct of their businesses in the manner described in the Time of Sale Prospectus and the Prospectus; (ii) the Intellectual Property Rights licensed to the Company and its Subsidiary, are valid, subsisting and enforceable, and there is no pending or, to the Company's knowledge, threatened action, suit, proceeding or claim by others challenging the validity, scope, inventorship, ownership or enforceability of any such Intellectual Property Rights; (iii) neither the Company nor its Subsidiary has received any notice alleging any infringement, misappropriation or other violation of Intellectual Property Rights; (iv) to the Company's knowledge, no third party is infringing, misappropriating or otherwise violating, or has infringed, misappropriated or otherwise violated, any Intellectual Property Rights owned by the Company that would materially adversely affect the Company and its Subsidiary, taken as a whole; (v) neither the Company nor its Subsidiary infringes, misappropriates or otherwise violates (including, if the Company's product candidates described in the Time of Sale Prospectus were manufactured, marketed, used or sold as of the date hereof) in any material respect, or has infringed, misappropriated or otherwise violated, any right or valid patent claim of any third party in any material respect; (vi) all employees, consultants or contractors engaged in the development of Intellectual Property Rights on behalf of the Company or its Subsidiary have executed an invention assignment agreement whereby such employees, consultants or contractors presently assign all of their right, title and interest in and to such Intellectual Property Rights to the Company or its Subsidiary, and to the Company's knowledge no such agreement has been breached or violated in any material respect; (vii) the Company and its Subsidiary use, and have used, commercially reasonable efforts to appropriately maintain all information intended to be maintained as a trade secret; (viii) to the knowledge of the Company, none of the Intellectual Property Rights of the Company have been obtained or are being used by the Company in material violation of any contractual obligation binding on the Company or, to the knowledge of the Company, upon any of its officers, consultants, directors or employees; (ix) the

Intellectual Property Rights owned or purported to be owned by the Company are free and clear of all material liens or encumbrances; (x) no third party, including any academic or governmental organization, possesses rights to the Intellectual Property Rights of the Company which, if exercised, could enable such party to develop, market or sell products competitive with those of the Company or to license a third party to so develop, market or sell products competitive with those of the Company; (xi) except as described in the Time of Sale Prospectus, the Company is not obligated to pay a material royalty, grant a license to, obtain a license from or provide other material consideration to any third party in connection with the Intellectual Property Rights of the Company; and (xii) all patents and patent applications owned by or licensed to the Company and included within the Intellectual Property Rights, to the knowledge of the Company, have been duly and properly filed, prosecuted and maintained.

(x) (i) The Company and its Subsidiary have complied and are presently in compliance with all internal and external privacy policies, contractual obligations, industry standards, applicable laws, statutes, judgments, orders, rules and regulations of any court or arbitrator or other governmental or regulatory authority with jurisdiction over the Company, in each case, relating to the collection, use, transfer, import, export, storage, protection, disposal and disclosure by the Company or its Subsidiary of personal, personally identifiable, household, sensitive, confidential or regulated data (“**Data Security Obligations**”, and such data, “**Confidential Data**”); (ii) the Company has not received any notification of or complaint regarding and is unaware of any other facts that, individually or in the aggregate, would reasonably indicate material non-compliance with any Data Security Obligation; and (iii) there is no action, suit or proceeding by or before any court or governmental agency, authority or body pending or, to the Company’s knowledge, threatened alleging material non-compliance with any Data Security Obligation.

(y) The Company and its Subsidiary’s information technology assets and equipment, computers, systems, networks, hardware, software, websites, applications and databases used to process, store, maintain and operate data, information and functions are adequate for, and operate and perform in all material respects as required in connection with, the operation of the business of the Company and the Subsidiary as currently conducted. The Company and its Subsidiary have taken all reasonable technical and organizational measures to protect the information technology systems and Confidential Data used in connection with the operation of the Company’s and its Subsidiary’s businesses. Without limiting the foregoing, the Company and its Subsidiary have used reasonable efforts to establish and maintain, and have established, maintained, implemented and complied with, reasonable information technology, information security, cyber security and data protection controls, policies and procedures, including oversight, access controls, encryption, technological and physical safeguards and business continuity/disaster recovery and security plans that are designed to protect against and prevent breach, destruction, loss, unauthorized distribution, use, access, disablement, misappropriation or modification, or other

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compromise or misuse of or relating to any information technology system or Confidential Data used in connection with the operation of the Company’s and its Subsidiary’s businesses (“**Breach**”). Except as disclosed in the Time of Sale Prospectus and the Prospectus, there has been no material Breach, and the Company and its Subsidiary have not been notified of, and have no knowledge of any event or condition that would reasonably be expected to result in, any material Breach.

(z) No material labor dispute with the employees of the Company or its Subsidiary exists, except as described in the Time of Sale Prospectus, or, to the knowledge of the Company, is imminent; and the Company is not aware of any existing, threatened or imminent labor disturbance by the employees of any of its principal suppliers, manufacturers or contractors that could have a material adverse effect on the Company and its Subsidiary, taken as a whole.

(aa) Except (i) as described in the Time of Sale Prospectus or (ii) as would not, singly or in the aggregate, reasonably be expected to have a material adverse effect on the Company and its Subsidiary, taken as a whole, each employee benefit plan, within the meaning of Section 3(3) of the Employee Retirement Income Security Act of 1974, as amended (“**ERISA**”), that the Company or any member of its “Controlled Group” (defined as any organization which is under common control with the Company within the meaning of Section 414 of the Internal Revenue Code of 1986, as amended (the “**Code**”)) sponsors or maintains has been maintained, in all material respects, in compliance with its terms and the requirements of any applicable statutes, orders, rules and regulations, including but not limited to ERISA and the Code.

(bb) The Company and its Subsidiary are insured by insurers of recognized financial responsibility against such losses and risks and in such amounts as, in the Company’s judgment, are prudent and customary in the businesses in which they are engaged; neither the Company nor its Subsidiary has been refused any insurance coverage sought or applied for; and neither the Company nor its Subsidiary has any reason to believe that it will not be able to renew its existing insurance coverage as and when such coverage expires or to obtain similar coverage from similar insurers as may be necessary to continue its business at a cost that would not reasonably be expected to have a material adverse effect on the Company and its Subsidiary, taken as a whole, except as described in the Time of Sale Prospectus.

(cc) The Company and its Subsidiary possess all certificates, authorizations and permits issued by the appropriate federal, state or foreign regulatory authorities necessary to conduct their respective businesses, and neither the Company nor its Subsidiary has received any notice of proceedings relating to the revocation or modification of any such certificate, authorization or permit which, singly or in the aggregate, if the subject of an unfavorable decision, ruling or finding, would have a material adverse effect on the Company and its Subsidiary, taken as a whole, except as described in the Time of Sale Prospectus.

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(dd) The Company and its Subsidiary (i) are and at all times have been, in all material respects, in compliance with all statutes, rules, and regulations applicable to the ownership, research, testing, development, manufacture, packaging, processing, use, storage, import, export or disposal of any product candidates of the Company or its Subsidiary, including, without limitation, the Federal Food, Drug and Cosmetic Act (21 U.S.C. § 301 et seq.), the regulations promulgated pursuant to such laws, and any successor government programs, and comparable state laws, and all other local, state, federal, and foreign laws, rules, regulations, policies and final administrative guidance relating to the regulation of the Company (collectively, the “**Applicable Regulatory Laws**”); (ii) possess all licenses, exemptions, certificates, approvals, consents, clearances, authorizations, permits, registrations and supplements or amendments thereto required by any such Applicable Regulatory Laws (“**Regulatory Authorizations**”) and such Regulatory Authorizations are valid and in full force and effect; (iii) are in compliance, in all material respects, with and are not in violation of, or in default under, any such Regulatory Authorization, and to the Company’s knowledge, no event has occurred which allows, or after notice or lapse of time would allow, revocation, termination or modification of any Regulatory Authorization or result in any other material impairment of the rights of the holder of any Regulatory Authorization, and the Company does not have any reason to believe that any Regulatory Authorization will not be renewed in the ordinary course; (iv) have not received written notice that any court or arbitrator or governmental or regulatory authority has taken, is taking, or intends to take action to limit, suspend, modify or revoke any Regulatory Authorizations nor, to the Company’s knowledge, is any such limitation, suspension, modification or revocation threatened; (v) have not received any notice of any claim, action, suit, proceeding, hearing, enforcement, investigation, arbitration or other action, or any U.S. Food and Drug Administration (“**FDA**”) Form 483, notice of adverse finding, warning letter, untitled letter or other communication from any court or arbitrator or governmental or regulatory authority alleging or asserting non-compliance with any Applicable Regulatory Laws or Regulatory Authorizations, nor, to the Company’s knowledge, is any such claim, action, suit, proceeding, hearing, enforcement, investigation, arbitration or other action or communication threatened; (vi) have filed, obtained, maintained or submitted all material reports, documents, forms, notices, applications, records, claims, submissions and supplements or amendments as required by any Applicable Regulatory Laws or Regulatory Authorizations, and all such reports, documents, forms, notices, applications, records, claims, submissions and supplements or amendments were complete and accurate on the date filed in all material respects (or were corrected or supplemented by a subsequent submission); and (vii) are not a party to any corporate integrity agreements, monitoring agreements, consent decrees, settlement orders, or similar agreements with or imposed by any governmental or regulatory authority.

(ee) All clinical and pre-clinical trials conducted by or on behalf of, or sponsored by, the Company or its Subsidiary, or in which the Company or its Subsidiary have participated, that are described or referred to in the Registration

Statement and the Time of Sale Prospectus were and, if still pending, are being conducted, in all material respects, in compliance with the experimental protocols established for such trials, with accepted medical and scientific standards, and with all Applicable Regulatory Laws, including regulations relating to Good Clinical Practices and Good Laboratory Practices, and all Regulatory Authorizations. The descriptions of the clinical and pre-clinical trials, including the results thereof, contained in the Registration Statement and the Time of Sale Prospectus are accurate and complete in all material respects and fairly present the data derived from such trials in all material respects; and neither the Company nor its Subsidiary is aware of any other clinical or pre-clinical trials, the results of which reasonably call into question the results described in the Registration Statement and the Time of Sale Prospectus. Neither the Company nor its Subsidiary have received any notices or correspondence from FDA or similar foreign, state, and local governmental or regulatory authorities (collectively, the “**Regulatory Authorities**”) or institutional review boards or comparable authorities requiring the termination, suspension, material modification or clinical hold of any clinical or pre-clinical trials conducted by or on behalf of the Company, and to the Company’s knowledge, there are no reasonable grounds for the same.

(ff) Neither the Company nor the Subsidiary, or any of their respective directors, officers, employees or, to the Company’s knowledge, agents, is or has been debarred, suspended or excluded, or has been convicted of any crime or engaged in any conduct that would result in debarment, suspension or exclusion by FDA or from any federal or state government health care program.

(gg) None of the Company’s or its Subsidiary’s product candidates has received marketing approval from any Regulatory Authority.

(hh) Ernst & Young LLP, which has certified certain financial statements of the Company and its Subsidiary, is an independent registered public accounting firm as required by the Securities Act and the rules and regulations of the Commission thereunder and the rules and regulations of the Public Company Accounting Oversight Board (United States).

(ii) The consolidated financial statements of the Company included in the Registration Statement, the Time of Sale Prospectus and the Prospectus, together with the related notes, present fairly in all material respects the financial position of the Company and its consolidated Subsidiary at the dates indicated and, in the case of the statements of operations, stockholders’ equity and cash flows of the Company and its consolidated Subsidiary, for the periods specified. The consolidated financial statements of the Company included in the Registration Statement, the Time of Sale Prospectus and the Prospectus comply in all material respects with the applicable requirements of the Securities Act and have been prepared in conformity with U.S. generally accepted accounting principles (“**GAAP**”) applied on a consistent basis throughout the periods involved except (i) the unaudited, interim financial statements, which are subject

to normal year-end adjustments and do not contain certain footnotes as permitted by the applicable rules of the Commission and (ii) as otherwise disclosed therein. Except as included therein, no supporting schedules are required to be included or incorporated by reference in the Registration Statement, the Time of Sale Prospectus or the Prospectus under the Securities Act and the rules and regulations of the Commission thereunder. All other financial information included in the Registration Statement, the Time of Sale Prospectus and the Prospectus has been derived from the accounting records of the Company and its consolidated Subsidiary and presents fairly in all material respects the information shown thereby.

(jj) The Company and its Subsidiary maintain a system of internal accounting controls sufficient to provide reasonable assurance that (i) transactions are executed in accordance with management's general or specific authorizations; (ii) transactions are recorded as necessary to permit preparation of financial statements in conformity with generally accepted accounting principles and to maintain asset accountability; (iii) access to assets is permitted only in accordance with management's general or specific authorization; and (iv) the recorded accountability for assets is compared with the existing assets at reasonable intervals and appropriate action is taken with respect to any differences. Except as described in the Time of Sale Prospectus, since the end of the Company's most recent audited fiscal year, there has been (i) no material weakness in the Company's internal control over financial reporting (whether or not remediated) and (ii) no change in the Company's internal control over financial reporting that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting.

(kk) The Company maintains disclosure controls and procedures (as such term is defined in Rule 13a-15(e) under the Securities Exchange Act of 1934, as amended (the "**Exchange Act**")) designed to comply with the requirements of the Exchange Act applicable to the Company. Such disclosure controls and procedures have been designed to ensure that material information relating to the Company is made known to the Company's principal executive officer and principal financial officer by others within the Company.

(ll) Except as described in the Time of Sale Prospectus, the Company has not sold, issued or distributed any shares of Common Stock during the six-month period preceding the date hereof, including any sales pursuant to Rule 144A under, or Regulation D or S of, the Securities Act, other than shares issued pursuant to employee benefit plans, qualified stock option plans or other employee compensation plans or pursuant to outstanding options, rights or warrants.

(mm) The Company and its Subsidiary have filed all federal, state, local and foreign tax returns required to be filed through the date of this Agreement or have requested extensions thereof (except where the failure to file would not, individually or in the aggregate, reasonably be expected to have a material

adverse effect) and have paid all taxes required to be paid thereon (except for cases in which the failure to file or pay would not reasonably be expected to have a material adverse effect, or, except as currently being contested in good faith and for which reserves required by GAAP have been created in the financial statements of the Company), and no tax deficiency has been determined adversely to the Company or its Subsidiary which has had (nor does the Company nor its Subsidiary have any notice or knowledge of any tax deficiency which would reasonably be expected to be determined adversely to the Company or its Subsidiary and which would reasonably be expected to have) a material adverse effect.

(nn) Other than its ownership of all of the equity interests of the Subsidiary, the Company does not, directly or indirectly, own capital stock or other equity or ownership or proprietary interests in any corporation, partnership, association, trust or other entity.

(oo) From the time of initial confidential submission of the Registration Statement to the Commission (or, if earlier, the first date on which the Company engaged directly or through any person authorized to act on its behalf in any Testing-the-Waters Communication) through the date hereof, the Company has been and is an “emerging growth company,” as defined in Section 2(a) of the Securities Act (an “**Emerging Growth Company**”). “**Testing-the-Waters Communication**” means any oral or written communication with potential investors undertaken in reliance on Section 5(d) of the Securities Act.

(pp) The Company (i) has not alone engaged in any Testing-the-Waters Communication other than Testing-the-Waters Communications with the consent of the Representatives with entities that are qualified institutional buyers within the meaning of Rule 144A under the Securities Act or institutions that are accredited investors within the meaning of Rule 501 under the Securities Act and (ii) has not authorized anyone other than the Representatives to engage in Testing-the-Waters Communications. The Company reconfirms that the Representatives have been authorized to act on its behalf in undertaking Testing-the-Waters Communications. The Company has not distributed any Written Testing-the-Waters Communications other than those listed on Schedule III hereto. “**Written Testing-the-Waters Communication**” means any Testing-the-Waters Communication that is a written communication within the meaning of Rule 405 under the Securities Act.

(qq) As of the time of each sale of the Shares in connection with the offering when the Prospectus is not yet available to prospective purchasers, none of (i) the Time of Sale Prospectus, (ii) any free writing prospectus, when considered together with the Time of Sale Prospectus, and (iii) any individual Written Testing-the-Waters Communication, when considered together with the Time of Sale Prospectus, included, includes or will include an untrue statement of a material fact or omitted, omits or will omit to state a material fact necessary in

order to make the statements therein, in the light of the circumstances under which they were made, not misleading.

(rr) Neither the Company nor its Subsidiary has any securities rated by any “nationally recognized statistical rating organization,” as such term is defined in Section 3(a)(62) of the Exchange Act.

2. *Agreements to Sell and Purchase.* The Company hereby agrees to sell to the several Underwriters, and each Underwriter, upon the basis of the representations and warranties herein contained, but subject to the conditions hereinafter stated, agrees, severally and not jointly, to purchase from the Company the respective numbers of Firm Shares set forth in Schedule I hereto opposite its name at \$[·] a share (the “**Purchase Price**”).

On the basis of the representations and warranties contained in this Agreement, and subject to its terms and conditions, the Company agrees to sell to the Underwriters the Additional Shares, and the Underwriters shall have the right to purchase, severally and not jointly, up to [·] Additional Shares at the Purchase Price, provided, however, that the amount paid by the Underwriters for any Additional Shares shall be reduced by an amount per share equal to any dividends declared by the Company and payable on the Firm Shares but not payable on such Additional Shares. The Representatives may exercise this right on behalf of the Underwriters in whole or from time to time in part by giving written notice not later than 30 days after the date of this Agreement. Any exercise notice shall specify the number of Additional Shares to be purchased by the Underwriters and the date on which such shares are to be purchased. Each purchase date must be at least one business day after the written notice is given and may not be earlier than the closing date for the Firm Shares nor later than ten business days after the date of such notice. Additional Shares may be purchased as provided in Section 4 hereof solely for the purpose of covering over-allotments made in connection with the offering of the Firm Shares. On each day, if any, that Additional Shares are to be purchased (an “**Option Closing Date**”), each Underwriter agrees, severally and not jointly, to purchase the number of Additional Shares (subject to such adjustments to eliminate fractional shares as the Representatives may determine) that bears the same proportion to the total number of Additional Shares to be purchased on such Option Closing Date as the number of Firm Shares set forth in Schedule I hereto opposite the name of such Underwriter bears to the total number of Firm Shares.

3. *Terms of Public Offering.* The Company is advised by the Representatives that the Underwriters propose to make a public offering of their respective portions of the Shares as soon after the Registration Statement and this Agreement have become effective as in the Representatives’ judgment is advisable. The Company is further advised by the Representatives that the Shares are to be offered to the public initially at \$[·] a share (the “**Public Offering Price**”) and to certain dealers selected by the Representatives at a price that represents a concession not in excess of \$[·] a share under the Public Offering Price, and that any Underwriter may allow, and such dealers may reallow, a concession, not in excess of \$[·] a share, to any Underwriter or to certain other dealers.

4. *Payment and Delivery.* Payment for the Firm Shares shall be made to the Company in Federal or other funds immediately available in New York City against delivery of such Firm Shares for the respective accounts of the several Underwriters at 10:00 a.m., New York City time, on [·], 2019, or at such other time on the same or such other date, not later than [·], 2019, as shall be designated in writing by the Representatives. The time and date of such payment are hereinafter referred to as the “**Closing Date.**”

Payment for any Additional Shares shall be made to the Company in Federal or other funds immediately available in New York City against delivery of such Additional Shares for the respective accounts of the several Underwriters at 10:00 a.m., New York City time, on the date specified in the corresponding notice described in Section 2 or at such other time on the same or on such other date, in any event not later than [·], 2019, as shall be designated in writing by the Representatives.

The Firm Shares and Additional Shares shall be registered in such names and in such denominations as the Representatives shall request in writing not later than one full business day prior to the Closing Date or the applicable Option Closing Date, as the case may be. The Firm Shares and Additional Shares shall be delivered to the Representatives on the Closing Date or an Option Closing Date, as the case may be, for the respective accounts of the several Underwriters, with any transfer taxes payable in connection with the transfer of the Shares to the Underwriters duly paid, against payment of the Purchase Price therefor.

5. *Conditions to the Underwriters’ Obligations.* The obligations of the Company to sell the Shares to the Underwriters and the several obligations of the Underwriters to purchase and pay for the Shares on the Closing Date are subject to the condition that the Registration Statement shall have become effective not later than [·] (New York City time) on the date hereof.

The several obligations of the Underwriters are subject to the following further conditions:

(a) Subsequent to the execution and delivery of this Agreement and prior to the Closing Date there shall not have occurred any change, or any development involving a prospective change, in the condition, financial or otherwise, or in the earnings, business or operations of the Company and its Subsidiary, taken as a whole, from that set forth in the Time of Sale Prospectus that, in the Representatives’ judgment, is material and adverse and that makes it, in the Representatives’ judgment, impracticable to market the Shares on the terms and in the manner contemplated in the Time of Sale Prospectus.

(b) The Underwriters shall have received on the Closing Date a certificate, dated the Closing Date and signed by an executive officer of the Company on behalf of the Company, to the effect set forth in Section 5(a) above; and to the effect that the representations and warranties of the Company contained in this Agreement are true and correct as of the Closing Date and that the

Company has complied with all of the agreements and satisfied all of the conditions on its part to be performed or satisfied hereunder on or before the Closing Date. The officer signing and delivering such certificate may rely upon the best of his or her knowledge as to the proceedings threatened.

(c) The Underwriters shall have received on the Closing Date an opinion and negative assurance letter from Wilmer Cutler Pickering Hale and Dorr LLP, outside counsel for the Company, dated the Closing Date, in form and substance reasonably satisfactory to the Underwriters.

(d) The Underwriters shall have received on the Closing Date an opinion of Cooley LLP, special counsel to the Company with respect to certain intellectual property matters, dated the Closing Date, in form and substance reasonably satisfactory to the Underwriters.

(e) The Underwriters shall have received on the Closing Date an opinion and negative assurance letter from Ropes & Gray LLP, counsel for the Underwriters, dated the Closing Date, in form and substance reasonably satisfactory to the Underwriters.

With respect to Sections 5(c) and 5(e) above, Wilmer Cutler Pickering Hale and Dorr LLP and Ropes & Gray LLP may state that their opinions and beliefs are based upon their participation in the preparation of the Registration Statement, the Time of Sale Prospectus and the Prospectus and any amendments or supplements thereto and review and discussion of the contents thereof, but are without independent check or verification, except as specified.

The opinions of Wilmer Cutler Pickering Hale and Dorr LLP and Cooley LLP described in Sections 5(c) and 5(d) above, respectively, shall be rendered to the Underwriters at the request of the Company and shall so state therein.

(f) The Underwriters shall have received, on each of the date hereof and the Closing Date, a letter dated the date hereof or the Closing Date, as the case may be, in form and substance satisfactory to the Underwriters, from Ernst & Young LLP, independent public accountants, containing statements and information of the type ordinarily included in accountants' "comfort letters" to underwriters with respect to the financial statements and certain financial information contained in the Registration Statement, the Time of Sale Prospectus and the Prospectus; *provided* that the letter delivered on the Closing Date shall use a "cut-off date" not earlier than the date hereof.

(g) The "lock-up" agreements, each substantially in the form of Exhibit A hereto, among the Representatives and each of the security holders, officers and directors of the Company, respectively, relating to sales and certain other dispositions of shares of Common Stock or certain other securities, delivered to the Representatives on or before the date hereof (the "**Lock-up Agreements**"), shall be in full force and effect on the Closing Date.

(h) Delivery to the Underwriters on the Closing Date of such other documents as the Representatives may reasonably request with respect to the good standing of the Company and the Subsidiary, the due authorization and issuance of the Firm Shares to be sold on the Closing Date and other matters related to the issuance of the Firm Shares.

(i) The several obligations of the Underwriters to purchase Additional Shares hereunder are subject to the delivery to the Underwriters on the applicable Option Closing Date of the following:

(i) a certificate, dated the Option Closing Date and signed by an executive officer of the Company on behalf of the Company, confirming that the certificate delivered on the Closing Date pursuant to Section 5(b) hereof remains true and correct as of such Option Closing Date;

(ii) an opinion and negative assurance letter from Wilmer Cutler Pickering Hale and Dorr LLP, outside counsel for the Company, dated the Option Closing Date, relating to the Additional Shares to be purchased on such Option Closing Date and otherwise to the same effect as the opinion required by Section 5(c) hereof;

(iii) an opinion of Cooley LLP, special counsel to the Company with respect to certain intellectual property matters, dated the Option Closing Date and otherwise to the same effect as the opinion required by Section 5(d) hereof;

(iv) an opinion and negative assurance letter from Ropes & Gray LLP, counsel for the Underwriters, dated the Option Closing Date, relating to the Additional Shares to be purchased on such Option Closing Date and otherwise to the same effect as the opinion required by Section 5(e) hereof;

(v) a letter dated the Option Closing Date, in form and substance satisfactory to the Underwriters, from Ernst & Young LLP, independent public accountants, substantially in the same form and substance as the letter furnished to the Underwriters pursuant to Section 5(f) hereof; *provided* that the letter delivered on the Option Closing Date shall use a “cut-off date” not earlier than two business days prior to such Option Closing Date; and

(vi) such other documents as the Representatives may reasonably request with respect to the good standing of the Company and its Subsidiary, the due authorization and issuance of the Additional Shares to be sold on such Option Closing Date and other matters related to the issuance of such Additional Shares.

6. *Covenants of the Company.* The Company covenants with each Underwriter as follows:

(a) To furnish to the Representatives, without charge, five signed copies of the Registration Statement (including exhibits thereto) and for delivery to each other Underwriter a conformed copy of the Registration Statement (without exhibits thereto) and to furnish to the Representatives in New York City, without charge, prior to 10:00 a.m. New York City time on the second business day succeeding the date of this Agreement and during the periods mentioned in Section 6(e) and 6(f) below, as many copies of the Time of Sale Prospectus, the Prospectus and any supplements and amendments thereto or to the Registration Statement as the Representatives may reasonably request.

(b) Before amending or supplementing the Registration Statement, the Time of Sale Prospectus or the Prospectus, to furnish to the Representatives a copy of each such proposed amendment or supplement and not to file any such proposed amendment or supplement to which the Representatives reasonably object in a timely manner, and to file with the Commission within the applicable period specified in Rule 424(b) under the Securities Act any prospectus required to be filed pursuant to such Rule.

(c) To furnish to the Representatives a copy of each proposed free writing prospectus to be prepared by or on behalf of, used by, or referred to by the Company and not to use or refer to any proposed free writing prospectus to which the Representatives reasonably object.

(d) Not to take any action that would result in an Underwriter or the Company being required to file with the Commission pursuant to Rule 433(d) under the Securities Act a free writing prospectus prepared by or on behalf of the Underwriter that the Underwriter otherwise would not have been required to file thereunder.

(e) If the Time of Sale Prospectus is being used to solicit offers to buy the Shares at a time when the Prospectus is not yet available to prospective purchasers and any event shall occur or condition exist as a result of which it is necessary to amend or supplement the Time of Sale Prospectus in order to make the statements therein, in the light of the circumstances under which they were made, not misleading, or if any event shall occur or condition exist as a result of which the Time of Sale Prospectus conflicts with the information contained in the Registration Statement then on file, or if, in the opinion of counsel for the Underwriters, it is necessary to amend or supplement the Time of Sale Prospectus to comply with applicable law, forthwith to prepare, file with the Commission and furnish, at its own expense, to the Underwriters and to any dealer upon request, either amendments or supplements to the Time of Sale Prospectus so that the statements in the Time of Sale Prospectus as so amended or supplemented will not, in the light of the circumstances when the Time of Sale Prospectus is delivered to a prospective purchaser, be misleading or so that the Time of Sale

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Prospectus, as amended or supplemented, will no longer conflict with the Registration Statement, or so that the Time of Sale Prospectus, as amended or supplemented, will comply with applicable law.

(f) If, during such period after the first date of the public offering of the Shares as in the opinion of counsel for the Underwriters the Prospectus (or in lieu thereof the notice referred to in Rule 173(a) of the Securities Act) is required by law to be delivered in connection with sales by an Underwriter or dealer, any event shall occur or condition exist as a result of which it is necessary to amend or supplement the Prospectus in order to make the statements therein, in the light of the circumstances when the Prospectus (or in lieu thereof the notice referred to in Rule 173(a) of the Securities Act) is delivered to a purchaser, not misleading, or if, in the opinion of counsel for the Underwriters, it is necessary to amend or supplement the Prospectus to comply with applicable law, forthwith to prepare, file with the Commission and furnish, at its own expense, to the Underwriters and to the dealers (whose names and addresses the Representatives will furnish to the Company) to which Shares may have been sold by the Representatives on behalf of the Underwriters and to any other dealers upon request, either amendments or supplements to the Prospectus so that the statements in the Prospectus as so amended or supplemented will not, in the light of the circumstances when the Prospectus (or in lieu thereof the notice referred to in Rule 173(a) of the Securities Act) is delivered to a purchaser, be misleading or so that the Prospectus, as amended or supplemented, will comply with applicable law.

(g) If required by applicable law, to endeavor to qualify the Shares for offer and sale under the securities or Blue Sky laws of such jurisdictions as the Representatives shall reasonably request; provided, however, that nothing contained herein shall require the Company to qualify to do business in any jurisdiction, to execute a general consent of service of process in any jurisdiction or to subject itself to taxation in any jurisdiction in which it is not otherwise subject.

(h) To make generally available to the Company's security holders and to the Representatives as soon as reasonably practicable an earning statement covering a period of at least twelve months beginning with the first fiscal quarter of the Company occurring after the date of this Agreement which shall satisfy the provisions of Section 11(a) of the Securities Act and the rules and regulations of the Commission thereunder; provided that the Company will be deemed to have furnished such statement to its security holders to the extent it is filed on the Commission's Electronic Data Gathering, Analysis and Retrieval System.

(i) Whether or not the transactions contemplated in this Agreement are consummated or this Agreement is terminated, to pay or cause to be paid all expenses incident to the performance of its obligations under this Agreement, including: (i) the fees, disbursements and expenses of the Company's counsel and the Company's accountants in connection with the registration and delivery of the Shares under the Securities Act and all other fees or expenses in connection with

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the preparation and filing of the Registration Statement, any preliminary prospectus, the Time of Sale Prospectus, the Prospectus, any free writing prospectus prepared by or on behalf of, used by, or referred to by the Company and amendments and supplements to any of the foregoing, including all printing costs associated therewith, and the mailing and delivering of copies thereof to the Underwriters and dealers, in the quantities hereinabove specified, (ii) all costs and expenses related to the transfer and delivery of the Shares to the Underwriters, including any transfer or other taxes payable thereon, (iii) the cost of printing or producing any Blue Sky or Legal Investment memorandum in connection with the offer and sale of the Shares under state securities laws and all expenses in connection with the qualification of the Shares for offer and sale under state securities laws as provided in Section 6(g) hereof, including filing fees and the reasonable and documented fees and disbursements of counsel for the Underwriters in connection with such qualification and in connection with the Blue Sky or Legal Investment memorandum (provided that the amount payable by the Company with respect to the fees and disbursements of counsel for the Underwriters pursuant to clause (iii) shall not exceed \$2,500), (iv) all filing fees and the reasonable fees and disbursements of counsel to the Underwriters incurred in connection with the review and qualification of the offering of the Shares by FINRA (provided that the amount payable by the Company with respect to the fees and disbursements of counsel for the Underwriters pursuant to clause (iv) shall not exceed \$30,000), (v) all fees and expenses in connection with the preparation and filing of the registration statement on Form 8-A relating to the Common Stock and all costs and expenses incident to listing the Shares on the Nasdaq Global Market, (vi) the cost of printing certificates representing the Shares, (vii) the costs and charges of any transfer agent, registrar or depository, (viii) the costs and expenses of the Company relating to investor presentations on any "road show" undertaken in connection with the marketing of the offering of the Shares, including, without limitation, expenses associated with the preparation or dissemination of any electronic road show, expenses associated with the production of road show slides and graphics, fees and expenses of any consultants engaged in connection with the road show presentations with the prior approval of the Company, travel and lodging expenses of the representatives and officers of the Company and any such consultants, and 50% of the cost of any aircraft or other transportation chartered in connection with the road show (the remaining 50% of the cost of such aircraft to be paid by the Underwriters), (ix) the document production charges and expenses associated with printing this Agreement and (x) all other costs and expenses incident to the performance of the obligations of the Company hereunder for which provision is not otherwise made in this Section. It is understood, however, that except as provided in this Section, Section 8 entitled "Indemnity and Contribution" and the last paragraph of Section 11 below, the Underwriters will pay all of their costs and expenses, including fees and disbursements of their counsel, stock transfer taxes payable on resale of any of the Shares by them and any advertising expenses connected with any offers they may make.

(j) The Company will promptly notify the Representatives if the Company ceases to be an Emerging Growth Company at any time prior to the later of (i) completion of the distribution of the Shares within the meaning of the Securities Act and (ii) completion of the Restricted Period (as defined in this Section 6).

(k) If at any time following the distribution of any Written Testing-the-Waters Communication there occurred or occurs an event or development as a result of which such Written Testing-the-Waters Communication included or would include an untrue statement of a material fact or omitted or would omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances existing at that subsequent time, not misleading, the Company will promptly notify the Representatives and will promptly amend or supplement, at its own expense, such Written Testing-the-Waters Communication to eliminate or correct such untrue statement or omission.

(l) The Company will deliver to each Underwriter (or its agent), on the date of execution of this Agreement, a properly completed and executed Certification Regarding Beneficial Owners of Legal Entity Customers, together with copies of identifying documentation, and the Company undertakes to provide such additional supporting documentation as each Underwriter may reasonably request in connection with the verification of the foregoing certification.

The Company also covenants with each Underwriter that, without the prior written consent of the Representatives on behalf of the Underwriters, it will not, and will not publicly disclose an intention to, during the period ending 180 days after the date of the Prospectus (the “**Restricted Period**”), (1) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend, or otherwise transfer or dispose of, directly or indirectly, any shares of Common Stock or any securities convertible into or exercisable or exchangeable for Common Stock or (2) enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the Common Stock, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of Common Stock or such other securities, in cash or otherwise, or (3) file any registration statement with the Commission relating to the offering of any shares of Common Stock or any securities convertible into or exercisable or exchangeable for Common Stock. The restrictions contained in this paragraph shall not apply to (a) the Shares to be sold hereunder, (b) the issuance by the Company of shares of Common Stock upon the exercise of an option or warrant or the conversion of a security outstanding on the date hereof and described in the Prospectus, (c) the grant by the Company of any options to purchase shares of Common Stock or other awards granted under a stock incentive plan or stock purchase plan described in the Prospectus, and the issuance by the Company of shares of Common Stock upon the exercise thereof, provided that the Company shall cause each recipient of such grant to execute and deliver to the Representatives an agreement substantially in the form of Exhibit A hereto if such recipient has not already delivered one, (d) the filing by the Company of any registration statement on Form S-8 or a successor form thereto relating to the shares of Common

Stock granted pursuant to or reserved for issuance under a stock incentive plan or stock purchase plan described in the Prospectus or (e) shares of Common Stock or other securities issued in connection with a joint venture, equipment leasing arrangement, licensing or collaboration transaction or other strategic transaction with an unaffiliated third party, provided that (x) the aggregate number of shares issued pursuant to this clause (e) shall not exceed 5% of the total number of outstanding shares of Common Stock immediately following the issuance and sale of the Shares to be sold hereunder and (y) the recipient of any such shares of Common Stock and securities issued pursuant to this clause (e) during the Restricted Period shall enter into an agreement substantially in the form of Exhibit A hereto.

If the Representatives, in their sole discretion, agree to release or waive the restrictions set forth in a Lock-up Agreement for an officer or director of the Company and provide the Company with notice of the impending release or waiver at least three business days before the effective date of the release or waiver, the Company agrees to announce the impending release or waiver by a press release substantially in the form of Exhibit B hereto through a major news service at least two business days before the effective date of the release or waiver.

7. *Covenants of the Underwriters.* Each Underwriter severally covenants with the Company not to take any action that would result in the Company being required to file with the Commission under Rule 433(d) a free writing prospectus prepared by or on behalf of such Underwriter that otherwise would not be required to be filed by the Company thereunder, but for the action of the Underwriter.

8. *Indemnity and Contribution.* (a) The Company agrees to indemnify and hold harmless each Underwriter, each person, if any, who controls any Underwriter within the meaning of either Section 15 of the Securities Act or Section 20 of the Exchange Act and each affiliate of any Underwriter within the meaning of Rule 405 under the Securities Act from and against any and all losses, claims, damages and liabilities (including, without limitation, any documented legal or other expenses reasonably incurred in connection with defending or investigating any such action or claim) that arise out of, relate to or are based upon any untrue statement or alleged untrue statement of a material fact contained in the Registration Statement or any amendment thereof, any preliminary prospectus, the Time of Sale Prospectus or any amendment or supplement thereto, any issuer free writing prospectus as defined in Rule 433(h) under the Securities Act, any Company information that the Company has filed, or is required to file, pursuant to Rule 433(d) under the Securities Act, any road show as defined in Rule 433(h) under the Securities Act (a "road show"), the Prospectus or any amendment or supplement thereto, or any Written Testing-the-Waters Communication caused by any omission or alleged omission to state therein a material fact required to be stated therein or necessary to make the statements therein not misleading, except insofar as such losses, claims, damages or liabilities are caused by any such untrue statement or omission or alleged untrue statement or omission based upon information relating to any Underwriter furnished to the Company in writing by such Underwriter through the Representatives expressly for use therein.

(b) Each Underwriter agrees, severally and not jointly, to indemnify and hold harmless the Company, its directors, its officers who sign the Registration Statement and each person, if any, who controls the Company within the meaning of either Section 15 of the Securities Act or Section 20 of the Exchange Act to the same extent as the foregoing indemnity from the Company to such Underwriter, but only with reference to information relating to such Underwriter furnished to the Company in writing by such Underwriter through the Representatives expressly for use in the Registration Statement, any preliminary prospectus, the Time of Sale Prospectus, any issuer free writing prospectus, road show or the Prospectus or any amendment or supplement thereto.

(c) In case any proceeding (including any governmental investigation) shall be instituted involving any person in respect of which indemnity may be sought pursuant to Section 8(a) or 8(b), such person (the “**indemnified party**”) shall promptly notify the person against whom such indemnity may be sought (the “**indemnifying party**”) in writing and the indemnifying party, upon request of the indemnified party, shall retain counsel reasonably satisfactory to the indemnified party to represent the indemnified party and any others the indemnifying party may designate in such proceeding and shall pay the reasonably incurred fees and disbursements of such counsel related to such proceeding. In any such proceeding, any indemnified party shall have the right to retain its own counsel, but the fees and expenses of such counsel shall be at the expense of such indemnified party unless (i) the indemnifying party and the indemnified party shall have mutually agreed to the retention of such counsel or (ii) the named parties to any such proceeding (including any impleaded parties) include both the indemnifying party and the indemnified party and representation of both parties by the same counsel would be inappropriate due to actual or potential differing interests between them. It is understood that the indemnifying party shall not, in respect of the legal expenses of any indemnified party in connection with any proceeding or related proceedings in the same jurisdiction, be liable for the fees and expenses of more than one separate firm (in addition to any local counsel) for all such indemnified parties and that all such fees and expenses shall be reimbursed as they are incurred upon receipt from the indemnified party of a written request for payment thereof. Such firm shall be designated in writing by the Representatives, in the case of parties indemnified pursuant to Section 8(a), and by the Company, in the case of parties indemnified pursuant to Section 8(b). The indemnifying party shall not be liable for any settlement of any proceeding effected without its written consent, but if settled with such consent or if there be a final judgment for the plaintiff, the indemnifying party agrees to indemnify the indemnified party from and against any loss or liability by reason of such settlement or judgment. Notwithstanding the foregoing sentence, if at any time an indemnified party shall have requested an indemnifying party to reimburse the indemnified party for fees and expenses of counsel as contemplated by the second and third sentences of this paragraph, the indemnifying party agrees that it shall be liable for any settlement of any proceeding effected without its written consent if (i) such settlement is entered into more than 30 days after receipt by such indemnifying party of the aforesaid request and (ii) such indemnifying party shall

not have reimbursed the indemnified party in accordance with such request prior to the date of such settlement. No indemnifying party shall, without the prior written consent of the indemnified party, effect any settlement of any pending or threatened proceeding in respect of which any indemnified party is or could have been a party and indemnity could have been sought hereunder by such indemnified party, unless such settlement (x) includes an unconditional release of such indemnified party from all liability on claims that are the subject matter of such proceeding and (y) does not include a statement admitting fault, culpability or a failure to act, by or on behalf of any indemnified party.

(d) To the extent the indemnification provided for in Section 8(a) or 8(b) is unavailable to an indemnified party or insufficient in respect of any losses, claims, damages or liabilities referred to therein, then each indemnifying party under such paragraph, in lieu of indemnifying such indemnified party thereunder, shall contribute to the amount paid or payable by such indemnified party as a result of such losses, claims, damages or liabilities (i) in such proportion as is appropriate to reflect the relative benefits received by the Company on the one hand and the Underwriters on the other hand from the offering of the Shares or (ii) if the allocation provided by clause 8(d)(i) above is not permitted by applicable law, in such proportion as is appropriate to reflect not only the relative benefits referred to in clause 8(d)(i) above but also the relative fault of the Company on the one hand and of the Underwriters on the other hand in connection with the statements or omissions that resulted in such losses, claims, damages or liabilities, as well as any other relevant equitable considerations. The relative benefits received by the Company on the one hand and the Underwriters on the other hand in connection with the offering of the Shares shall be deemed to be in the same respective proportions as the net proceeds from the offering of the Shares (before deducting expenses) received by the Company and the total underwriting discounts and commissions received by the Underwriters, in each case as set forth in the table on the cover of the Prospectus, bear to the aggregate Public Offering Price of the Shares. The relative fault of the Company on the one hand and the Underwriters on the other hand shall be determined by reference to, among other things, whether the untrue or alleged untrue statement of a material fact or the omission or alleged omission to state a material fact relates to information supplied by the Company or by the Underwriters and the parties' relative intent, knowledge, access to information and opportunity to correct or prevent such statement or omission. The Underwriters' respective obligations to contribute pursuant to this Section 8 are several in proportion to the respective number of Shares they have purchased hereunder, and not joint.

(e) The Company and the Underwriters agree that it would not be just or equitable if contribution pursuant to this Section 8 were determined by *pro rata* allocation (even if the Underwriters were treated as one entity for such purpose) or by any other method of allocation that does not take account of the equitable considerations referred to in Section 8(d). The amount paid or payable by an indemnified party as a result of the losses, claims, damages and liabilities referred to in Section 8(d) shall be deemed to include, subject to the limitations set forth

above, any legal or other expenses reasonably incurred by such indemnified party in connection with investigating or defending any such action or claim. Notwithstanding the provisions of this Section 8, no Underwriter shall be required to contribute any amount in excess of the amount by which the total underwriting discounts and commissions received by such Underwriter with respect to the Shares underwritten by it and distributed to the public exceeds the amount of any damages that such Underwriter has otherwise been required to pay by reason of such untrue or alleged untrue statement or omission or alleged omission. No person guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the Securities Act) shall be entitled to contribution from any person who was not guilty of such fraudulent misrepresentation. The remedies provided for in this Section 8 are not exclusive and shall not limit any rights or remedies which may otherwise be available to any indemnified party at law or in equity.

(f) The indemnity and contribution provisions contained in this Section 8 and the representations, warranties and other statements of the Company contained in this Agreement shall remain operative and in full force and effect regardless of (i) any termination of this Agreement, (ii) any investigation made by or on behalf of any Underwriter, any person controlling any Underwriter or any affiliate of any Underwriter or by or on behalf of the Company, its officers or directors or any person controlling the Company and (iii) acceptance of and payment for any of the Shares.

9. [Reserved.]

10. *Termination.* The Underwriters may terminate this Agreement by notice given by the Representatives to the Company, if after the execution and delivery of this Agreement and prior to the Closing Date (i) trading generally shall have been suspended or materially limited on, or by, as the case may be, either the New York Stock Exchange or the Nasdaq Global Market, (ii) trading of any securities of the Company shall have been suspended on any exchange or in any over-the-counter market, (iii) a material disruption in securities settlement, payment or clearance services in the United States shall have occurred, (iv) any moratorium on commercial banking activities shall have been declared by Federal or New York State authorities or (v) there shall have occurred any outbreak or escalation of hostilities, or any change in financial markets or any calamity or crisis that, in the Representatives' judgment, is material and adverse and which, singly or together with any other event specified in this clause (v), makes it, in the Representatives' judgment, impracticable or inadvisable to proceed with the offer, sale or delivery of the Shares on the terms and in the manner contemplated in the Time of Sale Prospectus or the Prospectus.

11. *Effectiveness; Defaulting Underwriters.* This Agreement shall become effective upon the execution and delivery hereof by the parties hereto.

If, on the Closing Date or an Option Closing Date, as the case may be, any one or more of the Underwriters shall fail or refuse to purchase Shares that it has or they have agreed to purchase hereunder on such date, and the aggregate number of Shares which

such defaulting Underwriter or Underwriters agreed but failed or refused to purchase is not more than one-tenth of the aggregate number of the Shares to be purchased on such date, the other Underwriters shall be obligated severally in the proportions that the number of Firm Shares set forth opposite their respective names in Schedule I bears to the aggregate number of Firm Shares set forth opposite the names of all such non-defaulting Underwriters, or in such other proportions as the Representatives may specify, to purchase the Shares which such defaulting Underwriter or Underwriters agreed but failed or refused to purchase on such date; *provided* that in no event shall the number of Shares that any Underwriter has agreed to purchase pursuant to this Agreement be increased pursuant to this Section 11 by an amount in excess of one-ninth of such number of Shares without the written consent of such Underwriter. If, on the Closing Date, any Underwriter or Underwriters shall fail or refuse to purchase Firm Shares and the aggregate number of Firm Shares with respect to which such default occurs is more than one-tenth of the aggregate number of Firm Shares to be purchased on such date, and arrangements satisfactory to the Representatives and the Company for the purchase of such Firm Shares are not made within 36 hours after such default, this Agreement shall terminate without liability on the part of any non-defaulting Underwriter or the Company. In any such case either the Representatives or the Company shall have the right to postpone the Closing Date, but in no event for longer than seven days, in order that the required changes, if any, in the Registration Statement, in the Time of Sale Prospectus, in the Prospectus or in any other documents or arrangements may be effected. If, on an Option Closing Date, any Underwriter or Underwriters shall fail or refuse to purchase Additional Shares and the aggregate number of Additional Shares with respect to which such default occurs is more than one-tenth of the aggregate number of Additional Shares to be purchased on such Option Closing Date, the non-defaulting Underwriters shall have the option to (i) terminate their obligation hereunder to purchase the Additional Shares to be sold on such Option Closing Date or (ii) purchase not less than the number of Additional Shares that such non-defaulting Underwriters would have been obligated to purchase in the absence of such default. Any action taken under this paragraph shall not relieve any defaulting Underwriter from liability in respect of any default of such Underwriter under this Agreement.

If this Agreement shall be terminated by the Underwriters, or any of them, because of any failure or refusal on the part of the Company to comply with the terms or to fulfill any of the conditions of this Agreement, or if for any reason the Company shall be unable to perform its obligations under this Agreement, other than by reason of a default by the Underwriters or following termination of this Agreement pursuant to clauses (i), (iii), (iv) or (v) of Section 10, the Company will reimburse the Underwriters or such Underwriters as have so terminated this Agreement with respect to themselves, severally, for all out-of-pocket expenses (including the reasonably incurred fees and disbursements of their counsel) reasonably incurred by such Underwriters in connection with this Agreement or the offering contemplated hereunder.

12. *Entire Agreement.* (a) This Agreement, together with any contemporaneous written agreements and any prior written agreements (to the extent not superseded by this Agreement) that relate to the offering of the Shares, represents the entire agreement between the Company and the Underwriters with respect to the preparation of any

preliminary prospectus, the Time of Sale Prospectus, the Prospectus, the conduct of the offering, and the purchase and sale of the Shares.

(b) The Company acknowledges that in connection with the offering of the Shares: (i) the Underwriters have acted at arm's length, are not agents of, and owe no fiduciary duties to, the Company or any other person, (ii) the Underwriters owe the Company only those duties and obligations set forth in this Agreement and prior written agreements (to the extent not superseded by this Agreement), if any, (iii) the Underwriters may have interests that differ from those of the Company and (iv) the Underwriters are not advising the Company or any other person as to any legal, tax, investment, accounting or regulatory matters in any jurisdiction. The Company waives to the full extent permitted by applicable law any claims it may have against the Underwriters arising from an alleged breach of fiduciary duty in connection with the offering of the Shares.

13. *Recognition of the U.S. Special Resolution Regimes.* (a) In the event that any Underwriter that is a Covered Entity becomes subject to a proceeding under a U.S. Special Resolution Regime, the transfer from such Underwriter of this Agreement, and any interest and obligation in or under this Agreement, will be effective to the same extent as the transfer would be effective under the U.S. Special Resolution Regime if this Agreement, and any such interest and obligation, were governed by the laws of the United States or a state of the United State.

(b) In the event that any Underwriter that is a Covered Entity or a BHC Act Affiliate of such Underwriter becomes subject to a proceeding under a U.S. Special Resolution Regime, Default Rights under this Agreement that may be exercised against such Underwriter are permitted to be exercised to no greater extent than such Default Rights could be exercised under the U.S. Special Resolution Regime if this Agreement were governed by the laws of the United States or a state of the United States.

For purposes of this Section a "**BHC Act Affiliate**" has the meaning assigned to the term "affiliate" in, and shall be interpreted in accordance with, 12 U.S.C. § 1841(k). "**Covered Entity**" means any of the following: (i) a "covered entity" as that term is defined in, and interpreted in accordance with, 12 C.F.R. § 252.82(b); (ii) a "covered bank" as that term is defined in, and interpreted in accordance with, 12 C.F.R. § 47.3(b); or (iii) a "covered FSI" as that term is defined in, and interpreted in accordance with, 12 C.F.R. § 382.2(b). "**Default Right**" has the meaning assigned to that term in, and shall be interpreted in accordance with, 12 C.F.R. §§ 252.81, 47.2 or 382.1, as applicable. "**U.S. Special Resolution Regime**" means each of (i) the Federal Deposit Insurance Act and the regulations promulgated thereunder and (ii) Title II of the Dodd-Frank Wall Street Reform and Consumer Protection Act and the regulations promulgated thereunder.

14. *Counterparts.* This Agreement may be signed in two or more counterparts, each of which shall be an original, with the same effect as if the signatures thereto and hereto were upon the same instrument.

15. *Applicable Law.* This Agreement shall be governed by and construed in accordance with the internal laws of the State of New York.

16. *Headings.* The headings of the sections of this Agreement have been inserted for convenience of reference only and shall not be deemed a part of this Agreement.

17. *Notices.* All communications hereunder shall be in writing and effective only upon receipt and if to the Underwriters shall be delivered, mailed or sent to the Representatives in care of Morgan Stanley & Co. LLC, 1585 Broadway, New York, New York 10036, Attention: Equity Syndicate Desk, with a copy to the Legal Department; in care of BofA Securities, Inc., One Bryant Park, New York, New York 10036, Attention: Syndicate Department, facsimile: 646-855-3073, with a copy to ECM Legal, facsimile: 212-230-8730; in care of SVB Leerink LLC, One Federal Street, 37th Floor, Boston, Massachusetts 02110, Attention: John I. Fitzgerald, Esq., facsimile: 617-918-4664 and, in each case, with a copy (which copy shall not constitute notice) to Ropes & Gray LLP, Prudential Tower, 800 Boylston Street, Boston, Massachusetts, 02199, Attention: Patrick O'Brien; and if to the Company shall be delivered, mailed or sent to Fulcrum Therapeutics, Inc., 26 Landsdowne Street, Cambridge, Massachusetts 02139, Attention: Chief Executive Officer, with a copy (which copy shall not constitute notice) to Wilmer Cutler Pickering Hale and Dorr LLP, 60 State Street, Boston, Massachusetts 02109, Attention: Lia Der Marderosian.

[Remainder of page intentionally left blank]

Very truly yours,

Fulcrum Therapeutics, Inc.

By: _____
Name:
Title:

Accepted as of the date hereof

Morgan Stanley & Co. LLC
BofA Securities, Inc.
SVB Leerink LLC

Acting severally on behalf of themselves and the several Underwriters
named in Schedule I hereto.

By: Morgan Stanley & Co. LLC

By: _____
Name:
Title:

By: BofA Securities, Inc.

By: _____
Name:
Title:

By: SVB Leerink LLC

By: _____
Name:
Title:

Underwriter	Number of Firm Shares To Be Purchased
Morgan Stanley & Co. LLC	[•]
BofA Securities, Inc.	[•]
SVB Leerink LLC	[•]
Total:	[•]

Time of Sale Prospectus

II-1

Written Testing-the-Waters Communications

III-1

FORM OF LOCK-UP LETTER

, 2019

Morgan Stanley & Co. LLC
Merrill Lynch, Pierce, Fenner & Smith Incorporated
SVB Leerink LLC

c/o Morgan Stanley & Co. LLC
1585 Broadway
New York, New York 10036

c/o Merrill Lynch, Pierce, Fenner & Smith Incorporated
One Bryant Park
New York, New York 10036

c/o SVB Leerink LLC
One Federal Street, 37th Floor
Boston, Massachusetts 02110

Ladies and Gentlemen:

The undersigned understands that Morgan Stanley & Co. LLC, Merrill Lynch, Pierce, Fenner & Smith Incorporated and SVB Leerink LLC (the “**Representatives**”) propose to enter into an Underwriting Agreement (the “**Underwriting Agreement**”) with Fulcrum Therapeutics, Inc., a Delaware corporation (the “**Company**”), providing for the public offering (the “**Public Offering**”) by the several Underwriters, including the Representatives (the “**Underwriters**”), of shares of the common stock, par value \$0.001 per share, of the Company (the “**Common Stock**”).

To induce the Underwriters that may participate in the Public Offering to continue their efforts in connection with the Public Offering, the undersigned hereby agrees that, without the prior written consent of each of the Representatives on behalf of the Underwriters, it will not, during the period commencing on the date hereof and ending 180 days after the date of the final prospectus (the “**Restricted Period**”) relating to the Public Offering (the “**Prospectus**”), (1) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend, or otherwise transfer or dispose of, directly or indirectly, any shares of Common Stock beneficially owned (as such term is used in Rule 13d-3 of the Securities Exchange Act of 1934, as amended (the “**Exchange Act**”), by the undersigned or any other securities so owned convertible into or exercisable or exchangeable for Common Stock or make any public announcement of its intention to do any of the foregoing or (2) enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the Common Stock,

whether any such transaction described in clause (1) or (2) above is to be settled by delivery of Common Stock or such other securities, in cash or otherwise. The foregoing shall not apply to:

(a) transactions relating to shares of Common Stock or other securities acquired in the Public Offering (other than any issuer-directed shares of Common Stock purchased in the Public Offering by an officer or director of the Company) or in open market transactions after the completion of the Public Offering, *provided* that no filing under Section 16(a) of the Exchange Act shall be required or shall be voluntarily made in connection with subsequent sales of Common Stock or other securities acquired in such open market transactions;

(b) (i) transfers of shares of Common Stock or any security convertible into or exercisable or exchangeable for Common Stock as a bona fide gift or gifts, or (ii) to a charitable organization or educational institution in a transaction not involving a disposition for value;

(c) transfers of shares of Common Stock or any security convertible into or exercisable or exchangeable for Common Stock to any member of the immediate family of the undersigned or any trust for the direct or indirect benefit of the undersigned or the immediate family of the undersigned in a transaction not involving a disposition for value;

(d) transfers of shares of Common Stock or any security convertible into or exercisable or exchangeable for Common Stock (i) by will, other testamentary document or intestate succession to the legal representative, heir, beneficiary or a member of the immediate family of the undersigned upon the death of the undersigned or (ii) solely by operation of law pursuant to a qualified domestic order or in connection with a divorce settlement;

(e) if the undersigned is an entity, transfers or distributions of shares of Common Stock or any security convertible into Common Stock to general or limited partners, members or stockholders of the undersigned, its direct or indirect affiliates (as defined in Rule 405 promulgated under the Securities Act of 1933, as amended) or to an investment fund or other entity that controls or manages, or is under common control with, the undersigned;

provided that in the case of any transfer, disposition or distribution pursuant to clause (b), (c), (d) or (e), (i) each transferee, donee or distributee shall sign and deliver a lock-up agreement substantially in the form of this agreement and (ii) no filing under Section 16(a) of the Exchange Act, reporting a reduction in beneficial ownership of shares of Common Stock, shall be required or shall be voluntarily made during the Restricted Period (other than, in the case of a transfer or other disposition pursuant to clause (c) above, any Form 4 or Form 5 required to be filed under the Exchange Act if the undersigned is subject to Section 16 reporting with respect to the Company under the Exchange Act and indicating by footnote disclosure or otherwise the nature of the transfer or disposition);

(f) transfers or dispositions of shares of Common Stock or any security convertible into or exercisable or exchangeable for Common Stock to the Company pursuant to any contractual arrangement in effect on the date of this agreement and disclosed to the Underwriters that provides for the repurchase of the undersigned's Common Stock or other securities by the Company or in connection with the termination of the undersigned's employment with or service to the Company; *provided* that no filing under Section 16(a) of the Exchange Act reporting a reduction in beneficial ownership of shares of Common Stock, shall be required or shall be voluntarily made during the Restricted Period in connection with any such transfers or dispositions (other than any Form 4 or Form 5 required to be filed under the Exchange Act if the undersigned is subject to Section 16 reporting with respect to the Company under the Exchange Act and indicating by footnote disclosure or otherwise the nature of the transfer or disposition);

(g) the conversion of outstanding shares of preferred stock of the Company described in the Prospectus and outstanding as of the date of the Prospectus into shares of Common Stock as described in the Prospectus, *provided* that the shares of Common Stock received upon conversion shall be subject to the restrictions set forth herein;

(h) the exercise of stock options to purchase shares of Common Stock granted under plans described in the Prospectus and any related transfer to the Company of shares of Common Stock (including by way of "net" or "cashless" exercise solely to cover withholding tax obligations in connection with such exercise and any transfer to the Company for the payment of taxes as a result of such exercise); *provided* that any shares of Common Stock received upon exercise shall be subject to the restrictions on transfer set forth in this agreement; *provided, further*, that no filing under Section 16(a) of the Exchange Act reporting a reduction in beneficial ownership of shares of Common Stock shall be required or shall be voluntarily made during the Restricted Period (other than a filing on a Form 4 that reports such disposition under the transaction code "F");

(i) the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of shares of Common Stock, *provided* that (i) such plan does not provide for the transfer of Common Stock during the Restricted Period and (ii) to the extent a public announcement or filing under the Exchange Act, if any, is required of or voluntarily made by or on behalf of the undersigned or the Company regarding the establishment of such plan, such announcement or filing shall include a statement to the effect that no transfer of Common Stock may be made under such plan during the Restricted Period; or

(j) (i) transfers of shares of Common Stock (or any securities convertible into or exercisable or exchangeable for Common Stock) pursuant to a bona fide third-party tender offer for shares of the Company's capital stock made to all holders of the Company's securities, merger, consolidation or other similar transaction approved by the Company's board of directors the result of which is that any person (as defined in Section 13(d)(3) of the Exchange Act), or group of persons, other than the Company, becomes the beneficial owner (as defined in Rules 13d-3 and 13d-5 of the Exchange Act) of more than 50% of the total voting power of the voting stock of the Company and (ii) entry into any lock-up, voting or similar agreement pursuant to which the undersigned may agree to

transfer, sell, tender or otherwise dispose of shares of Common Stock or such other securities in connection with a transaction described in (i) above); *provided* that in the event that such change of control transaction is not completed, the Common Stock (or any security convertible into or exercisable or exchangeable for Common Stock) owned by the undersigned shall remain subject to the restrictions contained in this agreement.

For purposes of this agreement, “immediate family” shall mean any relationship by blood, marriage, domestic partnership or adoption, not more remote than first cousin.

In addition, the undersigned agrees that, without the prior written consent of each of the Representatives on behalf of the Underwriters, it will not, during the Restricted Period, make any demand for or exercise any right with respect to, the registration of any shares of Common Stock or any security convertible into or exercisable or exchangeable for Common Stock; *provided* that the undersigned may make a demand under any registration rights agreement with the Company described in the Prospectus for, and exercise its rights under any such registration rights agreement with respect to, the registration after the expiration of the Restricted Period of shares of Common Stock that does not require the filing of any registration statement or any public announcement or activity regarding such registration during the Restricted Period (and no such public announcement or activity shall be voluntarily made or taken by the undersigned during the Restricted Period). The undersigned also agrees and consents to the entry of stop transfer instructions with the Company’s transfer agent and registrar against the transfer of the undersigned’s shares of Common Stock except in compliance with the foregoing restrictions.

If the undersigned is an officer or director of the Company, the undersigned further agrees that the foregoing provisions shall be equally applicable to any issuer-directed shares of Common Stock the undersigned may purchase in the Public Offering.

If the undersigned is an officer or director of the Company, (i) each of the Representatives agrees that, at least three business days before the effective date of any release or waiver of the foregoing restrictions in connection with a transfer of shares of Common Stock, the Representatives will notify the Company of the impending release or waiver, and (ii) the Company will agree in the Underwriting Agreement to announce the impending release or waiver by press release through a major news service at least two business days before the effective date of the release or waiver. Any release or waiver granted by the Representatives hereunder to any such officer or director shall only be effective two business days after the publication date of such press release. The provisions of this paragraph will not apply if (a) the release or waiver is effected solely to permit a transfer not for consideration and (b) the transferee has agreed in writing to be bound by the same terms described in this agreement to the extent and for the duration that such terms remain in effect at the time of the transfer.

The undersigned understands that the Company and the Underwriters are relying upon this agreement in proceeding toward consummation of the Public Offering. The undersigned further understands that this agreement is irrevocable and shall be binding upon the undersigned’s heirs, legal representatives, successors and assigns.

Whether or not the Public Offering actually occurs depends on a number of factors, including market conditions. Any Public Offering will only be made pursuant to an Underwriting Agreement, the terms of which are subject to negotiation between the Company and the Underwriters.

The undersigned understands that, (i) if either the Representatives, on the one hand, or the Company, on the other hand, informs the other in writing, prior to the execution of the Underwriting Agreement, that it has determined not to proceed with the Public Offering, (ii) if the Underwriting Agreement (other than the provisions thereof which survive termination) shall terminate or be terminated prior to payment for and delivery of the securities to be sold thereunder, (iii) if the registration statement related to the Public Offering has been withdrawn prior to the execution of the Underwriting Agreement or (iv) the Underwriting Agreement is not executed on or before October 31, 2019, then, in each case, this agreement shall automatically, and without any action on the part of any other party, be of no further force and effect, and the undersigned shall be automatically released from all obligations under this agreement.

This agreement and any claim, controversy or dispute arising under or related to this agreement shall be governed by and construed in accordance with the laws of the State of New York, without regard to the conflict of laws principles thereof.

Very truly yours,

(Name)

(Address)

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EXHIBIT B

FORM OF WAIVER OF LOCK-UP

, 20

[Name and Address of
Officer or Director
Requesting Waiver]

Dear Mr./Ms. [Name]:

This letter is being delivered to you in connection with the offering by Fulcrum Therapeutics, Inc., a Delaware corporation (the “**Company**”), of shares of common stock, \$0.001 par value (the “**Common Stock**”), of the Company and the lock-up letter dated , 2019 (the “**Lock-up Letter**”), executed by you in connection with such offering, and your request for a [waiver] [release] dated , 20 , with respect to shares of Common Stock (the “**Shares**”).

Each of Morgan Stanley & Co. LLC, BofA Securities, Inc. and SVB Leerink LLC hereby agrees to [waive] [release] the transfer restrictions set forth in the Lock-up Letter, but only with respect to the Shares, effective , 20 ; provided, however, that such [waiver] [release] is conditioned on the Company announcing the impending [waiver] [release] by press release through a major news service at least two business days before effectiveness of such [waiver] [release]. This letter will serve as notice to the Company of the impending [waiver] [release].

Except as expressly [waived] [released] hereby, the Lock-up Letter shall remain in full force and effect.

[Remainder of page intentionally left blank]

B-1

Very truly yours,

Morgan Stanley & Co. LLC
BofA Securities, Inc.
SVB Leerink LLC

Acting severally on behalf of themselves and the several Underwriters named
in Schedule I to the Underwriting Agreement

By: Morgan Stanley & Co. LLC

By: _____
Name:
Title:

By: BofA Securities, Inc.

By: _____
Name:
Title:

By: SVB Leerink LLC

By: _____
Name:
Title:

cc: Fulcrum Therapeutics, Inc.

FORM OF PRESS RELEASE

Fulcrum Therapeutics, Inc.
[Date]

Fulcrum Therapeutics, Inc. (the “**Company**”) announced today that Morgan Stanley & Co. LLC, BofA Securities, Inc. and SVB Leerink LLC, the joint lead book-running managers in the Company’s recent public sale of shares of common stock are [waiving][releasing] a lock-up restriction with respect to shares of the Company’s common stock held by [lock-up counterparty], a [description of lock-up counterparty] of the Company. The [waiver][release] will take effect on , 20 , and the shares may be sold on or after such date.

This press release is not an offer for sale of the securities in the United States or in any other jurisdiction where such offer is prohibited, and such securities may not be offered or sold in the United States absent registration or an exemption from registration under the United States Securities Act of 1933, as amended.

AMENDED AND RESTATED
CERTIFICATE OF INCORPORATION

OF

FULCRUM THERAPEUTICS, INC.

(Pursuant to Sections 242 and 245 of the
General Corporation Law of the State of Delaware)

Fulcrum Therapeutics, Inc., a corporation organized and existing under and by virtue of the provisions of the General Corporation Law of the State of Delaware (the “**General Corporation Law**”),

DOES HEREBY CERTIFY:

1. That the name of this corporation is Fulcrum Therapeutics, Inc., and that this corporation was originally incorporated pursuant to the General Corporation Law on August 18, 2015.
2. That the Board of Directors duly adopted resolutions proposing to amend and restate the Amended and Restated Certificate of Incorporation of this corporation, as amended, declaring said amendment and restatement to be advisable and in the best interests of this corporation and its stockholders, and authorizing the appropriate officers of this corporation to solicit the consent of the stockholders therefor, which resolution setting forth the proposed amendment and restatement is as follows:

RESOLVED, that the Amended and Restated Certificate of Incorporation of this corporation, as amended, be amended and restated in its entirety to read as follows:

FIRST: The name of this corporation is Fulcrum Therapeutics, Inc. (the “**Corporation**”)

SECOND: The address of the registered office of the Corporation in the State of Delaware is Corporation Trust Center, 1209 Orange Street, in the City of Wilmington, New Castle County, Delaware 19801. The name of its registered agent at such address is The Corporation Trust Company.

THIRD: The nature of the business or purposes to be conducted or promoted is to engage in any lawful act or activity for which corporations may be organized under the General Corporation Law.

FOURTH: (i) The total number of shares of all classes of stock which the Corporation shall have authority to issue is 135,000,000 shares of Common Stock, \$0.001 par value per share (“**Common Stock**”) and 100,000,000 shares of Preferred Stock, \$0.001 par value per share (“**Preferred Stock**”).

The following is a statement of the designations and the powers, privileges and rights, and the qualifications, limitations or restrictions thereof in respect of each class of capital stock of the Corporation.

A. COMMON STOCK

1. General. The voting, dividend and liquidation rights of the holders of the Common Stock are subject to and qualified by the rights, powers and preferences of the holders of the Preferred Stock set forth herein.

2. Voting. The holders of the Common Stock are entitled to one vote for each share of Common Stock held at all meetings of stockholders (and written actions in lieu of meetings); provided, however, that, except as otherwise required by law, holders of Common Stock, as such, shall not be entitled to vote on any amendment to the Corporation's Amended and Restated Certificate of Incorporation (the "**Certificate of Incorporation**") that relates solely to the terms of one or more outstanding series of Preferred Stock if the holders of such affected series are entitled, either separately or together with the holders of one or more other such series, to vote thereon pursuant to the Certificate of Incorporation or pursuant to the General Corporation Law. The number of authorized shares of Common Stock may be increased or decreased (but not below the number of shares thereof then outstanding) by (in addition to any vote of the holders of one or more series of Preferred Stock that may be required by the terms of the Certificate of Incorporation) the affirmative vote of the holders of shares of capital stock of the Corporation representing a majority of the votes represented by all outstanding shares of capital stock of the Corporation entitled to vote, irrespective of the provisions of Section 242(b)(2) of the General Corporation Law.

B. PREFERRED STOCK

Preferred Stock may be issued from time to time in one or more series, each of such series to consist of such number of shares and to have such terms, rights, powers and preferences, and the qualifications and limitations with respect thereto, as stated or expressed herein.

60,000,000 shares of the authorized Preferred Stock of the Corporation are hereby designated "**Series A Preferred Stock**" and 40,000,000 shares of the authorized Preferred Stock of the Corporation are hereby designated "**Series B Preferred Stock**", each such series with the following rights, preferences, powers, privileges and restrictions, qualifications and limitations. Unless otherwise indicated, references to "Sections" or "Subsections" in this Part B of this Article Fourth refer to sections and subsections of Part B of this Article Fourth.

1. Dividends. From and after the date of the issuance of any shares of Series B Preferred Stock, dividends at the rate per annum of \$0.16 per share shall accrue on such shares of Series B Preferred Stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series B Preferred Stock) (the "**Series B Accruing Dividends**"). From and after the date of the issuance of any shares of Series A Preferred Stock, dividends at the rate per annum of \$0.08 per share shall accrue on such shares of Series A Preferred Stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series A

Preferred Stock) (the “**Series A Accruing Dividends**”, and collectively with the Series B Accruing Dividends, the “**Preferred Accruing Dividends**”). The Preferred Accruing Dividends shall accrue from day to day, whether or not declared, shall be cumulative and shall be paid on a *pari passu* basis; provided however, that the Preferred Accruing Dividends shall be payable solely in accordance with the following sentence or upon liquidation, dissolution or winding up of the Corporation or a Deemed Liquidation Event (as defined below) in accordance with Subsection 2.1 or Subsection 2.3.2(b). The Corporation shall not declare, pay or set aside any dividends on shares of any other class or series of capital stock of the Corporation (other than dividends on shares of Common Stock payable in shares of Common Stock) unless (in addition to the obtaining of any consents required elsewhere in the Certificate of Incorporation) the holders of the Series A Preferred Stock and the Series B Preferred Stock then outstanding shall first receive, or simultaneously receive, a dividend on each outstanding share of Preferred Stock, with the Series A Preferred Stock and the Series B Preferred Stock being treated on a *pari passu* basis, in an amount at least equal to the greater of (i) the amount of the aggregate Preferred Accruing Dividends then accrued on such share of Preferred Stock, as applicable, and not previously paid and (ii) (A) in the case of a dividend on Common Stock or any class or series that is convertible into Common Stock, that dividend per share of Preferred Stock as would equal the product of (1) the dividend payable on each share of such class or series determined, if applicable, as if all shares of such class or series had been converted into Common Stock and (2) the number of shares of Common Stock issuable upon conversion of a share of the applicable series of Preferred Stock, in each case calculated on the record date for determination of holders entitled to receive such dividend or (B) in the case of a dividend on any class or series that is not convertible into Common Stock, at a rate per share of Preferred Stock determined by (1) dividing the amount of the dividend payable on each share of such class or series of capital stock by the original issuance price of such class or series of capital stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to such class or series) and (2) multiplying such fraction by an amount equal to the Series A Original Issue Price (as defined below) or the Series B Original Issue Price (as defined below), as applicable; provided that, if the Corporation declares, pays or sets aside, on the same date, a dividend on shares of more than one class or series of capital stock of the Corporation, the dividend payable to the holders of a series of Preferred Stock pursuant to this Section 1 shall be calculated based upon the dividend on the class or series of capital stock that would result in the highest Preferred Stock dividend for such series. The “**Series A Original Issue Price**” shall mean \$1.00 per share, subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series A Preferred Stock. The “**Series B Original Issue Price**” shall mean \$2.00 per share, subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series B Preferred Stock. The Series A Original Issue Price and Series B Original Issue Price shall each be referred to as a “**Preferred Stock Original Issue Price.**”

2. Liquidation, Dissolution or Winding Up; Certain Mergers, Consolidations and Asset Sales.

2.1 Preferential Payments to Holders of Series A Preferred Stock and Series B Preferred Stock. In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Corporation or Deemed Liquidation Event, the holders of shares of Series A Preferred Stock and Series B Preferred Stock then outstanding shall be entitled to be paid on a *pari passu*

basis out of the assets of the Corporation available for distribution to its stockholders before any payment shall be made to the holders of Common Stock by reason of their ownership thereof, an amount per share equal to the greater of (i) the applicable Preferred Stock Original Issue Price, plus any applicable Preferred Accruing Dividends accrued but unpaid thereon, whether or not declared, together with any other dividends declared but unpaid thereon or (ii) such amount per share as would have been payable had all shares of such series of Preferred Stock been converted into Common Stock pursuant to Section 4 immediately prior to such liquidation, dissolution, winding up or Deemed Liquidation Event. If upon any such liquidation, dissolution or winding up of the Corporation or Deemed Liquidation Event, the assets of the Corporation available for distribution to its stockholders shall be insufficient to pay the holders of shares of Preferred Stock the full amount to which they shall be entitled under this Subsection 2.1, the holders of shares of Preferred Stock shall share ratably in any distribution of the assets available for distribution in proportion to the respective amounts which would otherwise be payable in respect of the shares held by them upon such distribution if all amounts payable on or with respect to such shares were paid in full. The amount which a holder of a share of Series A Preferred Stock is entitled to receive under this Subsection 2.1 is hereinafter referred to as the “**Series A Liquidation Amount**.” The amount which a holder of a share of Series B Preferred Stock is entitled to receive under this Subsection 2.1 is hereinafter referred to as the “**Series B Liquidation Amount**.” Each of the Series A Liquidation Amount and Series B Liquidation Amount is hereinafter referred to as a “**Preferred Stock Liquidation Amount**.”

2.2 Distribution of Remaining Assets. In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Corporation or Deemed Liquidation Event, after the payment of all preferential amounts required to be paid to the holders of shares of Preferred Stock, the remaining assets of the Corporation available for distribution to its stockholders shall be distributed among the holders of the shares of Common Stock, pro rata based on the number of shares held by each such holder.

2.3 Deemed Liquidation Events.

2.3.1 Definition. Each of the following events shall be considered a “**Deemed Liquidation Event**” unless the holders of at least 65% in interest of the then outstanding shares of Preferred Stock, voting together as a single class and on an as-converted basis (the “**Required Vote**”), elect otherwise by written notice sent to the Corporation at least ten (10) days prior to the effective date of any such event:

- (a) a merger or consolidation in which
 - (i) the Corporation is a constituent party or
 - (ii) a subsidiary of the Corporation is a constituent party and the Corporation issues shares of its capital stock pursuant to such merger or consolidation,

except (A) any such merger or consolidation effected exclusively to change the domicile of the Corporation or (B) any such merger or consolidation involving the Corporation or a subsidiary in which the shares of capital stock of the Corporation outstanding immediately prior to such merger or consolidation continue to represent, or are converted into or exchanged for shares of capital

stock that represent, immediately following such merger or consolidation, a majority, by voting power, of the capital stock of (1) the surviving or resulting corporation or (2) if the surviving or resulting corporation is a wholly owned subsidiary of another corporation immediately following such merger or consolidation, the parent corporation of such surviving or resulting corporation; or

(b) the sale, lease, transfer, exclusive license or other disposition, in a single transaction or series of related transactions, by the Corporation or any subsidiary of the Corporation of all or substantially all the assets of the Corporation and its subsidiaries taken as a whole or the sale or disposition (whether by merger or otherwise) of one or more subsidiaries of the Corporation if substantially all of the assets of the Corporation and its subsidiaries taken as a whole are held by such subsidiary or subsidiaries, except where such sale, lease, transfer, exclusive license or other disposition is to a wholly owned subsidiary of the Corporation.

2.3.2 Effecting a Deemed Liquidation Event

(a) The Corporation shall not have the power to effect a Deemed Liquidation Event referred to in Subsection 2.3.1(a)(i) above unless the agreement or plan of merger or consolidation for such transaction (the “**Merger Agreement**”) provides that the consideration payable to the stockholders of the Corporation shall be allocated among the holders of capital stock of the Corporation in accordance with Subsections 2.1 and 2.2 above.

(b) In the event of a Deemed Liquidation Event referred to in Subsection 2.3.1(a)(ii), or 2.3.1(b) above, if the Corporation does not effect a dissolution of the Corporation under the General Corporation Law within ninety (90) days after such Deemed Liquidation Event, then (i) the Corporation shall send a written notice to each holder of Preferred Stock no later than the ninetieth (90th) day after the Deemed Liquidation Event advising such holders of their right (and the requirements to be met to secure such right) pursuant to the terms of the following clause (ii) to require the redemption of such shares of Preferred Stock, and (ii) if the holders representing the Required Vote so request in a written instrument delivered to the Corporation not later than one hundred twenty (120) days after such Deemed Liquidation Event, the Corporation shall use the consideration received by the Corporation for such Deemed Liquidation Event (net of any retained liabilities associated with the assets sold or technology licensed, as determined in good faith by the Board of Directors of the Corporation (the “**Board of Directors**”), together with any other assets of the Corporation available for distribution to its stockholders (the “**Available Proceeds**”), all to the extent permitted by Delaware law governing distributions to stockholders, on the one hundred fiftieth (150th) day after such Deemed Liquidation Event (the “**Redemption Date**”), to redeem all outstanding shares of Preferred Stock, on a *pari passu* basis, at a price per share equal to the applicable Preferred Stock Liquidation Amount (each, a “**Redemption Price**”). Notwithstanding the foregoing, in the event of a redemption pursuant to the preceding sentence, if the Available Proceeds are not sufficient to redeem all outstanding shares of Preferred Stock, the Corporation shall ratably redeem each holder’s shares of Preferred Stock, on a *pari passu* basis, to the fullest extent of such Available Proceeds and shall redeem the remaining shares as soon as it may lawfully do so under Delaware law governing distributions to stockholders. Prior to the distribution or redemption provided for in this Subsection 2.3.2(b), the Corporation shall not expend or dissipate the consideration received for such Deemed Liquidation

Event, except to discharge expenses incurred in connection with such Deemed Liquidation Event or in the ordinary course of business.

(c) The Corporation shall send written notice of a required redemption pursuant to Subsection 2.3.2(b) (the “Redemption Notice”) to each holder of record of Preferred Stock not less than forty (40) days prior to the Redemption Date. The Redemption Notice shall state:

(i) the number of shares and series of Preferred Stock held by the holder that the Corporation shall redeem on the Redemption Date;

(ii) the Redemption Date and the Redemption Price for each series of Preferred Stock;

(iii) the date upon which the holder’s right to convert such shares terminates (as determined in accordance with Subsection 4.1.2); and

(iv) for holders of shares in certificated form, that the holder is to surrender to the Corporation, in the manner and at the place designated, his, her or its certificate or certificates representing the shares of Preferred Stock to be redeemed.

(d) On or before the Redemption Date, each holder of shares of Preferred Stock, unless such holder has exercised his, her or its right to convert such shares as provided in Section 4.1, shall, if a holder of shares in certificated form, surrender the certificate or certificates representing such shares (or, if such registered holder alleges that such certificate has been lost, stolen or destroyed, a lost certificate affidavit and agreement reasonably acceptable to the Corporation to indemnify the Corporation against any claim that may be made against the Corporation on account of the alleged loss, theft or destruction of such certificate) to the Corporation, in the manner and at the place designated in the Redemption Notice, and thereupon the Redemption Price for such shares shall be payable to the order of the person whose name appears on such certificate or certificates as the owner thereof.

(e) If the Redemption Notice shall have been duly given, and if on the applicable Redemption Date the Redemption Price payable upon redemption of the shares of Preferred Stock to be redeemed on the Redemption Date is paid or tendered for payment or deposited with an independent payment agent so as to be available therefor in a timely manner, then notwithstanding that any certificates evidencing any of the shares of Preferred Stock so called for redemption shall not have been surrendered, dividends with respect to such shares of Preferred Stock shall cease to accrue after the Redemption Date and all rights with respect to such shares shall forthwith after the Redemption Date terminate, except only the right of the holders to receive the Redemption Price without interest upon surrender of any such certificate or certificates therefor.

2.3.3 Amount Deemed Paid or Distributed. If the amount deemed paid or distributed to the holders of capital stock of the Corporation upon any such merger, consolidation, sale, transfer, exclusive license, other disposition or redemption is made in property other than in cash, the value of such property paid or distributed to such holders by the Corporation or the

acquiring person, firm or other entity shall be the fair market value of such property, determined as follows:

(a) For securities not subject to investment letters or other similar restrictions on free marketability,

(i) if traded on a securities exchange, the value shall be deemed to be the average of the closing prices of the securities on such exchange or market over the 30-period ending three (3) days prior to the closing of such transaction;

(ii) if actively traded over-the-counter, the value shall be deemed to be the average of the closing bid prices over the 30-day period ending three (3) days prior to the closing of such transaction; or

(iii) if there is no active public market, the value shall be the fair market value thereof, as determined in good faith by the Board of Directors.

(b) The method of valuation of securities subject to investment letters or other similar restrictions on free marketability (other than restrictions arising solely by virtue of a stockholder's status as an affiliate or former affiliate) shall take into account an appropriate discount (as determined in good faith by the Board of Directors) from the market value as determined pursuant to clause (a) above so as to reflect the approximate fair market value thereof.

2.3.4 Allocation of Escrow or Contingent Payments. In the event of a Deemed Liquidation Event pursuant to Subsection 2.3.1(a)(i), if any portion of the consideration payable to the stockholders of the Corporation is payable only upon satisfaction of contingencies (the "**Additional Consideration**"), the Merger Agreement shall provide that (a) the portion of such consideration that is not Additional Consideration (such portion, the "**Initial Consideration**") shall be allocated among the holders of capital stock of the Corporation in accordance with Subsections 2.1 and 2.2 as if the Initial Consideration were the only consideration payable in connection with such Deemed Liquidation Event and (b) any Additional Consideration which becomes payable to the stockholders of the Corporation upon satisfaction of such contingencies shall be allocated among the holders of capital stock of the Corporation in accordance with Subsections 2.1 and 2.2 after taking into account the previous payment of the Initial Consideration as part of the same transaction. For the purposes of this Subsection 2.3.4, consideration placed into escrow or retained as holdback to be available for satisfaction of indemnification or similar obligations or otherwise subject to contingencies in connection with such Deemed Liquidation Event shall be deemed to be Additional Consideration.

3. Voting.

3.1 General. On any matter presented to the stockholders of the Corporation for their action or consideration at any meeting of stockholders of the Corporation (or by written consent of stockholders in lieu of a meeting), each holder of outstanding shares of Preferred Stock shall be entitled to cast the number of votes equal to the number of whole shares of Common Stock into which the shares of Preferred Stock held by such holder are convertible as of the record date for determining stockholders entitled to vote on such matter. Except as provided by law or by the

other provisions of the Certificate of Incorporation, holders of Preferred Stock shall vote together with the holders of Common Stock as a single class, on an as-converted basis.

3.2 Election of Directors. The holders of record of the shares of Series A Preferred Stock, exclusively and as a separate class, shall be entitled to elect one (1) director of the Corporation (the “**Series A Director**”). The holders of record of the shares of Series B Preferred Stock, exclusively and as a separate class, shall be entitled to elect one (1) director of the Corporation (the “**Series B Director**”). The Series A Director and the Series B Director shall be hereinafter referred to as the “**Preferred Directors**”. Any director elected as provided in the preceding sentences may be removed without cause by, and only by, the affirmative vote of the holders of the shares of the class or series of capital stock entitled to elect such director or directors, given either at a special meeting of such stockholders duly called for that purpose (or by a written consent of stockholders in lieu of a meeting). The holders of record of the shares of Common Stock and of any other class or series of voting stock (including the Preferred Stock), exclusively and voting together as a single class, shall be entitled to elect the balance of the total number of directors of the Corporation. At any meeting held for the purpose of electing a director, the presence in person or by proxy of the holders of a majority of the outstanding shares of the class or series entitled to elect such director shall constitute a quorum for the purpose of electing such director. A vacancy in any directorship filled by the holders of any class or series shall be filled only by vote or written consent in lieu of a meeting of the holders of such class or series or by any remaining director or directors elected by the holders of such class or series pursuant to this Subsection 3.2.

3.3 Preferred Stock Protective Provisions.

3.3.1 Preferred Stock Protective Provisions. At any time when any shares of Preferred Stock are outstanding, the Corporation or any of its subsidiaries shall not, either directly or indirectly by amendment, merger, consolidation or otherwise, do any of the following without (in addition to any other vote required by law or the Certificate of Incorporation) the written consent or affirmative vote of the holders representing the Required Vote, given in writing or by vote at a meeting, and any such act or transaction entered into without such consent or vote shall be null and void ab initio, and of no force or effect:

- (a) liquidate, dissolve or wind-up the business and affairs of the Corporation, effect any merger or consolidation or any other Deemed Liquidation Event, or consent to any of the foregoing;
- (b) amend, alter or repeal any provision of the Certificate of Incorporation or Bylaws of the Corporation;
- (c) create or authorize the creation of or issue or obligate itself to issue shares of, any other security convertible into or exercisable for any equity security having rights, preferences or privileges senior to or on parity with any series of Preferred Stock, or increase the authorized number of shares of Preferred Stock or of any additional class or series of capital stock unless it ranks junior to the Preferred Stock;

(d) reclassify, alter or amend any existing security that is junior to or on parity with the Preferred Stock, if such reclassification, alteration or amendment would render such other security senior to or on parity with the Preferred Stock;

(e) purchase or redeem or pay or declare any dividend or make any distribution on, any shares of capital stock prior to the Preferred Stock, other than stock repurchased from former employees, officers, directors or consultants in connection with the cessation of their employment/services, at the lower of fair market value or cost, or as approved by the Board of Directors, including the approval of at least one Preferred Director;

(f) create or authorize the creation of any debt security other than equipment leases or bank lines of credit unless such debt security has received the prior approval of the Board of Directors, including the approval of at least one Preferred Director;

(g) increase or decrease the authorized number of directors constituting the Board of Directors; or

(h) create or hold capital stock in any subsidiary that is not a wholly-owned subsidiary or dispose of any subsidiary stock or all or substantially all of any subsidiary assets.

3.3.2 Series B Preferred Stock Protective Provisions. At any time when any shares of Series B Preferred Stock are outstanding, the Corporation or any of its subsidiaries shall not, either directly or indirectly by amendment, merger, consolidation or otherwise, do any of the following without (in addition to any other vote required by law or the Certificate of Incorporation) the written consent or affirmative vote of the holders representing a majority in interest of the then outstanding shares of Series B Preferred Stock, voting together as a separate class (the “**Series B Required Vote**”), given in writing or by vote at a meeting, and any such act or transaction entered into without such consent or vote shall be null and void *ab initio*, and of no force or effect:

(a) amend or waive the rights, preferences or privileges of the Series B Preferred Stock in a manner that is adverse to the Series B Preferred Stock (provided that the creation or issuance of a new series of senior Preferred Stock shall not in and of itself trigger this provision);

(b) pay or declare any dividend or make any distribution on any shares of capital stock prior to the Series B Preferred Stock, except as set forth in Section 1; or

(c) increase or decrease the authorized number of shares of Series B Preferred Stock.

3.3.3 Series A Preferred Stock Protective Provisions. At any time when any shares of Series A Preferred Stock are outstanding, the Corporation or any of its subsidiaries shall not, either directly or indirectly by amendment, merger, consolidation or otherwise, do any of the following without (in addition to any other vote required by law or the Certificate of Incorporation) the written consent or affirmative vote of the holders representing a majority in interest of the then outstanding shares of Series A Preferred Stock, voting together as a separate

class (the “**Series A Required Vote**”), given in writing or by vote at a meeting, and any such act or transaction entered into without such consent or vote shall be null and void *ab initio*, and of no force or effect:

- (a) amend or waive the rights, preferences or privileges of the Series A Preferred Stock in a manner that is adverse to the Series A Preferred Stock (provided that the creation or issuance of a new series of senior Preferred Stock shall not in and of itself trigger this provision);
- (b) pay or declare any dividend or make any distribution on any shares of capital stock prior to the Series A Preferred Stock, except as set forth in Section 1; or
- (c) increase or decrease the authorized number of shares of Series A Preferred Stock.

4. Optional Conversion.

The holders of the Preferred Stock shall have conversion rights as follows (the “**Conversion Rights**”):

4.1 Right to Convert.

4.1.1 Conversion Ratio. Each share of Preferred Stock shall be convertible, at the option of the holder thereof, at any time and from time to time, and without the payment of additional consideration by the holder thereof, into such number of fully paid and nonassessable shares of Common Stock as is determined by dividing the applicable Preferred Stock Original Issue Price by the applicable Preferred Stock Conversion Price (as defined below) in effect at the time of conversion. The “**Series A Conversion Price**” shall initially be equal to \$1.00. Such initial Series A Conversion Price, and the rate at which shares of Series A Preferred Stock may be converted into shares of Common Stock, shall be subject to adjustment as provided below. The “**Series B Conversion Price**” shall initially be equal to \$2.00. Such initial Series B Conversion Price, and the rate at which shares of Series B Preferred Stock may be converted into shares of Common Stock, shall be subject to adjustment as provided below. The Series A Conversion Price and the Series B Conversion Price shall each be referred to as a “**Preferred Stock Conversion Price**” and together as the “**Preferred Stock Conversion Prices.**”

4.1.2 Termination of Conversion Rights. In the event of a notice of redemption of any shares of Preferred Stock pursuant to Subsection 2.3.2(b), the Conversion Rights of the shares designated for redemption shall terminate at the close of business on the last full day preceding the date fixed for redemption, unless the Redemption Price is not fully paid on such Redemption Date, in which case the Conversion Rights for such shares shall continue until such price is paid in full. In the event of a liquidation, dissolution or winding up of the Corporation or a Deemed Liquidation Event, the Conversion Rights shall terminate at the close of business on the last full day preceding the date fixed for the payment of any such amounts distributable on such event to the holders of Preferred Stock.

4.2 Fractional Shares. No fractional shares of Common Stock shall be issued upon conversion of the Preferred Stock. In lieu of any fractional shares to which the holder would

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otherwise be entitled, the Corporation shall pay cash equal to such fraction multiplied by the fair market value of a share of Common Stock as determined in good faith by the Board of Directors. Whether or not fractional shares would be issuable upon such conversion shall be determined on the basis of the total number of shares of Series A Preferred Stock or Series B Preferred Stock, as applicable, the holder is at the time converting into Common Stock and the aggregate number of shares of Common Stock issuable upon such conversion.

4.3 Mechanics of Conversion.

4.3.1 Notice of Conversion. In order for a holder of Preferred Stock to voluntarily convert shares of Preferred Stock into shares of Common Stock, such holder shall surrender the certificate or certificates for such shares of Preferred Stock (or, if such registered holder alleges that such certificate has been lost, stolen or destroyed, a lost certificate affidavit and agreement reasonably acceptable to the Corporation to indemnify the Corporation against any claim that may be made against the Corporation on account of the alleged loss, theft or destruction of such certificate), at the office of the transfer agent for the Preferred Stock (or at the principal office of the Corporation if the Corporation serves as its own transfer agent), together with written notice that such holder elects to convert all or any number of the shares of the Preferred Stock represented by such certificate or certificates and, if applicable, any event on which such conversion is contingent. Such notice shall state such holder’s name or the names of the nominees in which such holder wishes the certificate or certificates for shares of Common Stock to be issued. If required by the Corporation, certificates surrendered for conversion shall be endorsed or accompanied by a written instrument or instruments of transfer, in form satisfactory to the Corporation, duly executed by the registered holder or his, her or its attorney duly authorized in writing. The close of business on the date of receipt by the transfer agent (or by the Corporation if the Corporation serves as its own transfer agent) of such certificates (or lost certificate affidavit and agreement) and notice shall be the time of conversion (the “**Conversion Time**”), and the shares of Common Stock issuable upon conversion of the shares represented by such certificate shall be deemed to be outstanding of record as of such date. The Corporation shall, as soon as practicable after the Conversion Time, (i) issue and deliver to such holder of Preferred Stock, or to his, her or its nominees, a certificate or certificates for the number of full shares of Common Stock issuable upon such conversion in accordance with the provisions hereof and, a certificate for the number (if any) of the shares of Series A Preferred Stock or Series B Preferred Stock, as applicable, represented by the surrendered certificate that were not converted into Common Stock, (ii) pay in cash such amount as provided in Subsection 4.2 in lieu of any fraction of a share of Common Stock otherwise issuable upon such conversion, and (iii) pay all declared but unpaid dividends on the shares of Preferred Stock converted.

4.3.2 Reservation of Shares. The Corporation shall at all times when the Preferred Stock shall be outstanding, reserve and keep available out of its authorized but unissued capital stock, for the purpose of effecting the conversion of the Preferred Stock, such number of its duly authorized shares of Common Stock as shall from time to time be sufficient to effect the conversion of all outstanding Preferred Stock; and if at any time the number of authorized but unissued shares of Common Stock shall not be sufficient to effect the conversion of all then outstanding shares of the Preferred Stock, the Corporation shall take such corporate action as may be necessary to increase its authorized but unissued shares of Common Stock to such number of shares as shall be sufficient for such purposes, including, without limitation, engaging in best

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efforts to obtain the requisite stockholder approval of any necessary amendment to the Certificate of Incorporation. Before taking any action which would cause an adjustment reducing a Preferred Stock Conversion Price below the then par value of the shares of Common Stock issuable upon conversion of the applicable series of Preferred Stock, the Corporation will take any corporate action which may, in the opinion of its counsel, be necessary in order that the Corporation may validly and legally issue fully paid and nonassessable shares of Common Stock at such adjusted Preferred Stock Conversion Price.

4.3.3 Effect of Conversion. All shares of Preferred Stock which shall have been surrendered for conversion as herein provided shall no longer be deemed to be outstanding and all rights with respect to such shares shall immediately cease and terminate at the Conversion Time, except only the right of the holders thereof to receive shares of Common Stock in exchange therefor, to receive payment in lieu of any fraction of a share otherwise issuable upon such conversion as provided in Subsection 4.2 and to receive payment of any dividends declared but unpaid thereon. Any shares of Preferred Stock so converted shall be retired and cancelled and may not be reissued as shares of such series, and the Corporation may thereafter take such appropriate action (without the need for stockholder action) as may be necessary to reduce the authorized number of shares of Preferred Stock accordingly.

4.3.4 No Further Adjustment. Upon any such conversion, no adjustment to a Preferred Stock Conversion Price shall be made for any declared but unpaid dividends on the applicable series of Preferred Stock surrendered for conversion or on the Common Stock delivered upon conversion.

4.3.5 Taxes. The Corporation shall pay any and all issue and other similar taxes that may be payable in respect of any issuance or delivery of shares of Common Stock upon conversion of shares of Preferred Stock pursuant to this Section 4. The Corporation shall not, however, be required to pay any tax which may be payable in respect of any transfer involved in the issuance and delivery of shares of Common Stock in a name other than that in which the shares of Preferred Stock so converted were registered, and no such issuance or delivery shall be made unless and until the person or entity requesting such issuance has paid to the Corporation the amount of any such tax or has established, to the satisfaction of the Corporation, that such tax has been paid.

4.4 Adjustments to Preferred Stock Conversion Prices for Diluting Issues.

4.4.1 Special Definitions. For purposes of this Article Fourth, the following definitions shall apply:

(a) **“Option”** shall mean rights, options or warrants to subscribe for, purchase or otherwise acquire Common Stock or Convertible Securities.

(b) **“Series B Original Issue Date”** shall mean the date on which the first share of Series B Preferred Stock was issued.

(c) **“Convertible Securities”** shall mean any evidences of indebtedness, shares or other securities directly or indirectly convertible into or exchangeable for Common Stock, but excluding Options.

(d) **“Additional Shares of Common Stock”** shall mean all shares of Common Stock issued (or, pursuant to Subsection 4.4.3 below, deemed to be issued) by the Corporation after the Series B Original Issue Date, other than (1) the following shares of Common Stock and (2) shares of Common Stock deemed issued pursuant to the following Options and Convertible Securities (clauses (1) and (2), collectively **“Exempted Securities”**):

- (i) shares of Common Stock, Options or Convertible Securities issued as a dividend or distribution on Preferred Stock;
- (ii) shares of Common Stock actually issued upon the exercise of Options or the conversion or exchange of Convertible Securities, in each case provided such issuance is pursuant to the terms of such Option or Convertible Security;
- (iii) shares of Common Stock, Options or Convertible Securities issued by reason of a dividend, stock split, split-up or other distribution on shares of Common Stock that is covered by Subsections 4.5, 4.6, 4.7 or 4.8 below;
- (iv) shares of Common Stock or Options issued to employees or directors of, or consultants or advisors to, the Corporation or any of its subsidiaries pursuant to a plan, agreement or arrangement approved by the Board of Directors, including at least one Preferred Director;
- (v) shares of Common Stock, Options or Convertible Securities issued to banks, equipment lessors or other financial institutions, or to real property lessors, pursuant to a debt financing, equipment leasing or real property leasing transaction that is approved by the Board of Directors, including at least one Preferred Director, and that is primarily for non-equity financing purposes; and
- (vi) shares of Common Stock, Options or Convertible Securities issued in connection with sponsored research, collaboration, technology license, development, original equipment manufacturer, marketing or other similar agreements or strategic partnerships that are approved by the Board of Directors, including at least one Preferred Director, and that are primarily for non-equity financing purposes.

4.4.2 No Adjustment of Preferred Stock Conversion Prices. No adjustment in the Series A Conversion Price shall be made as the result of the issuance or deemed issuance of Additional Shares of Common Stock if the Corporation receives written notice from the holders representing the Series A Required Vote agreeing that no such adjustment shall be made as the result of the issuance or deemed issuance of such Additional Shares of Common Stock. No adjustment in the Series B Conversion Price shall be made as the result of the issuance or deemed issuance of Additional Shares of Common Stock if the Corporation receives written notice from the holders representing the Series B Required Vote agreeing that no such adjustment shall be made as the result of the issuance or deemed issuance of such Additional Shares of Common Stock.

4.4.3 Deemed Issue of Additional Shares of Common Stock.

(a) If the Corporation at any time or from time to time after the Series B Original Issue Date shall issue any Options or Convertible Securities (excluding Options or Convertible Securities which are themselves Exempted Securities) or shall fix a record date for the determination of holders of any class of securities entitled to receive any such Options or Convertible Securities, then the maximum number of shares of Common Stock (as set forth in the instrument relating thereto, assuming the satisfaction of any conditions to exercisability, convertibility or exchangeability but without regard to any provision contained therein for a subsequent adjustment of such number) issuable upon the exercise of such Options or, in the case of Convertible Securities and Options therefor, the conversion or exchange of such Convertible Securities, shall be deemed to be Additional Shares of Common Stock issued as of the time of such issue or, in case such a record date shall have been fixed, as of the close of business on such record date.

(b) If the terms of any Option or Convertible Security, the issuance of which resulted in an adjustment to a Preferred Stock Conversion Price pursuant to the terms of Subsection 4.4.4 below, are revised as a result of an amendment to such terms or if any other adjustment is made pursuant to the provisions of such Option or Convertible Security (but excluding automatic adjustments to such terms pursuant to anti-dilution or similar provisions of such Option or Convertible Security) to provide for either (1) any increase or decrease in the number of shares of Common Stock issuable upon the exercise, conversion and/or exchange of any such Option or Convertible Security or (2) any increase or decrease in the consideration payable to the Corporation upon such exercise, conversion and/or exchange, then, effective upon such increase or decrease becoming effective, the applicable Preferred Stock Conversion Price computed upon the original issue of such Option or Convertible Security (or upon the occurrence of a record date with respect thereto) shall be readjusted to such Preferred Stock Conversion Price as would have obtained had such revised terms been in effect upon the original date of issuance of such Option or Convertible Security. Notwithstanding the foregoing, no readjustment pursuant to this clause (b) shall have the effect of increasing any Preferred Stock Conversion Price to an amount which exceeds the lower of (i) the applicable Preferred Stock Conversion Price in effect immediately prior to the original adjustment made as a result of the issuance of such Option or Convertible Security, or (ii) the applicable Preferred Stock Conversion Price that would have resulted from any issuances of Additional Shares of Common Stock (other than deemed issuances of Additional Shares of Common Stock as a result of the issuance of such Option or Convertible Security) between the original adjustment date and such readjustment date.

(c) If the terms of any Option or Convertible Security (excluding Options or Convertible Securities which are themselves Exempted Securities), the issuance of which did not result in an adjustment to a Preferred Stock Conversion Price pursuant to the terms of Subsection 4.4.4 below (either because the consideration per share (determined pursuant to Subsection 4.4.5 hereof) of the Additional Shares of Common Stock subject thereto was equal to or greater than the applicable Preferred Stock Conversion Price then in effect, or because such Option or Convertible Security was issued before the Series B Original Issue Date), are revised after the Series B Original Issue Date as a result of an amendment to such terms or any other adjustment pursuant to the provisions of such Option or Convertible Security (but excluding automatic adjustments to such terms pursuant to anti-dilution or similar provisions of such Option or Convertible Security) to provide for either (1) any increase in the number of shares of Common Stock issuable upon the exercise, conversion or exchange of any such Option or Convertible

Security or (2) any decrease in the consideration payable to the Corporation upon such exercise, conversion or exchange, then such Option or Convertible Security, as so amended or adjusted, and the Additional Shares of Common Stock subject thereto (determined in the manner provided in Subsection 4.4.3(a) above) shall be deemed to have been issued effective upon such increase or decrease becoming effective.

(d) Upon the expiration or termination of any unexercised Option or unconverted or unexchanged Convertible Security (or portion thereof) which resulted (either upon its original issuance or upon a revision of its terms) in an adjustment to a Preferred Stock Conversion Price pursuant to the terms of Subsection 4.4.4 below, the applicable Preferred Stock Conversion Price shall be readjusted to the Preferred Stock Conversion Price as would have obtained had such Option or Convertible Security (or portion thereof) never been issued.

(e) If the number of shares of Common Stock issuable upon the exercise, conversion and/or exchange of any Option or Convertible Security, or the consideration payable to the Corporation upon such exercise, conversion and/or exchange, is calculable at the time such Option or Convertible Security is issued or amended but is subject to adjustment based upon subsequent events, any adjustment to the a Preferred Stock Conversion Price provided for in this Subsection 4.4.3 shall be effected at the time of such issuance or amendment based on such number of shares or amount of consideration without regard to any provisions for subsequent adjustments (and any subsequent adjustments shall be treated as provided in clauses (b) and (c) of this Subsection 4.4.3). If the number of shares of Common Stock issuable upon the exercise, conversion and/or exchange of any Option or Convertible Security, or the consideration payable to the Corporation upon such exercise, conversion and/or exchange, cannot be calculated at all at the time such Option or Convertible Security is issued or amended, any adjustment to the a Preferred Stock Conversion Price that would result under the terms of this Subsection 4.4.3 at the time of such issuance or amendment shall instead be effected at the time such number of shares and/or amount of consideration is first calculable (even if subject to subsequent adjustments), assuming for purposes of calculating such adjustment to such Preferred Stock Conversion Price that such issuance or amendment took place at the time such calculation can first be made.

4.4.4 Adjustment of Preferred Stock Conversion Prices Upon Issuance of Additional Shares of Common Stock. In the event the Corporation shall at any time or from time to time after the Series B Original Issue Date issue Additional Shares of Common Stock (including Additional Shares of Common Stock deemed to be issued pursuant to Subsection 4.4.3), without consideration or for a consideration per share less than a Preferred Stock Conversion Price in effect immediately prior to such issuance or deemed issuance, then such Preferred Stock Conversion Price shall be reduced, concurrently with such issue, to a price (calculated to the nearest one-hundredth of a cent) determined in accordance with the following formula:

$$CP_2 = CP_1 * (A + B) / (A + C).$$

For purposes of the foregoing formula, the following definitions shall apply:

(a) "CP₂" shall mean the applicable Preferred Stock Conversion Price in effect immediately after such issuance or deemed issuance of Additional Shares of Common Stock;

(b) “CP₁” shall mean the applicable Preferred Stock Conversion Price in effect immediately prior to such issuance or deemed issuance of Additional Shares of Common Stock;

(c) “A” shall mean the number of shares of Common Stock outstanding immediately prior to such issuance or deemed issuance of Additional Shares of Common Stock (treating for this purpose as outstanding all shares of Common Stock issuable upon exercise of Options outstanding immediately prior to such issuance or deemed issuance or upon conversion or exchange of Convertible Securities (including the Preferred Stock) outstanding (assuming exercise of any outstanding Options therefor) immediately prior to such issue);

(d) “B” shall mean the number of shares of Common Stock that would have been issued if such Additional Shares of Common Stock had been issued or deemed issued at a price per share equal to CP₁ (determined by dividing the aggregate consideration received by the Corporation in respect of such issue by CP₁); and

(e) “C” shall mean the number of such Additional Shares of Common Stock issued in such transaction.

4.4.5 Determination of Consideration. For purposes of this Subsection 4.4, the consideration received by the Corporation for the issuance or deemed issuance of any Additional Shares of Common Stock shall be computed as follows:

(a) Cash and Property: Such consideration shall:

(i) insofar as it consists of cash, be computed at the aggregate amount of cash received by the Corporation, excluding amounts paid or payable for accrued interest;

(ii) insofar as it consists of property other than cash, be computed at the fair market value thereof at the time of such issue, as determined in good faith by the Board of Directors, including at least one Preferred Director; and

(iii) in the event Additional Shares of Common Stock are issued together with other shares or securities or other assets of the Corporation for consideration which covers both, be the proportion of such consideration so received, computed as provided in clauses (i) and (ii) above, as determined in good faith by the Board of Directors, including at least one Preferred Director.

(b) Options and Convertible Securities. The consideration per share received by the Corporation for Additional Shares of Common Stock deemed to have been issued pursuant to Subsection 4.4.3, relating to Options and Convertible Securities, shall be determined by dividing

(i) the total amount, if any, received or receivable by the Corporation as consideration for the issue of such Options or Convertible Securities, plus the minimum aggregate amount of additional consideration (as set forth in the instruments relating thereto, without regard to any provision contained therein for a subsequent adjustment of such

consideration) payable to the Corporation upon the exercise of such Options or the conversion or exchange of such Convertible Securities, or in the case of Options for Convertible Securities, the exercise of such Options for Convertible Securities and the conversion or exchange of such Convertible Securities, by

(ii) the maximum number of shares of Common Stock (as set forth in the instruments relating thereto, without regard to any provision contained therein for a subsequent adjustment of such number) issuable upon the exercise of such Options or the conversion or exchange of such Convertible Securities, or in the case of Options for Convertible Securities, the exercise of such Options for Convertible Securities and the conversion or exchange of such Convertible Securities.

4.4.6 Multiple Closing Dates. In the event the Corporation shall issue on more than one date Additional Shares of Common Stock that are a part of one transaction or a series of related transactions and that would result in an adjustment to a Preferred Stock Conversion Price pursuant to the terms of Subsection 4.4.4 above then, upon the final such issuance, such Preferred Stock Conversion Price shall be readjusted to give effect to all such issuances as if they occurred on the date of the first such issuance (and without giving effect to any additional adjustments as a result of any such subsequent issuances within such period).

4.5 Adjustment for Stock Splits and Combinations. If the Corporation shall at any time or from time to time after the Series B Original Issue Date effect a subdivision of the outstanding Common Stock, the Preferred Stock Conversion Prices in effect immediately before that subdivision shall be proportionately decreased so that the number of shares of Common Stock issuable on conversion of each share of such series shall be increased in proportion to such increase in the aggregate number of shares of Common Stock outstanding. If the Corporation shall at any time or from time to time after the Series B Original Issue Date combine the outstanding shares of Common Stock, the Preferred Stock Conversion Prices in effect immediately before the combination shall be proportionately increased so that the number of shares of Common Stock issuable on conversion of each share of such series shall be decreased in proportion to such decrease in the aggregate number of shares of Common Stock outstanding. Any adjustment under this subsection shall become effective at the close of business on the date the subdivision or combination becomes effective.

4.6 Adjustment for Certain Dividends and Distributions. In the event the Corporation at any time or from time to time after the Series B Original Issue Date shall make or issue, or fix a record date for the determination of holders of Common Stock entitled to receive, a dividend or other distribution payable on the Common Stock in additional shares of Common Stock, then and in each such event the Preferred Stock Conversion Prices in effect immediately before such event shall be decreased as of the time of such issuance or, in the event such a record date shall have been fixed, as of the close of business on such record date, by multiplying the applicable Preferred Stock Conversion Price then in effect by a fraction:

- (1) the numerator of which shall be the total number of shares of Common Stock issued and outstanding immediately prior to the time of such issuance or the close of business on such record date, and

- (2) the denominator of which shall be the total number of shares of Common Stock issued and outstanding immediately prior to the time of such issuance or the close of business on such record date plus the number of shares of Common Stock issuable in payment of such dividend or distribution.

Notwithstanding the foregoing, (a) if such record date shall have been fixed and such dividend is not fully paid or if such distribution is not fully made on the date fixed therefor, the Preferred Stock Conversion Prices shall be recomputed accordingly as of the close of business on such record date and thereafter the Preferred Stock Conversion Prices shall be adjusted pursuant to this subsection as of the time of actual payment of such dividends or distributions; and (b) that no such adjustment shall be made if the holders of Preferred Stock simultaneously receive a dividend or other distribution of shares of Common Stock in a number equal to the number of shares of Common Stock as they would have received if all outstanding shares of Preferred Stock had been converted into Common Stock on the date of such event.

4.7 Adjustments for Other Dividends and Distributions. In the event the Corporation at any time or from time to time after the Series B Original Issue Date shall make or issue, or fix a record date for the determination of holders of Common Stock entitled to receive, a dividend or other distribution payable in securities of the Corporation (other than a distribution of shares of Common Stock in respect of outstanding shares of Common Stock) or in other property and the provisions of Section 1 do not apply to such dividend or distribution, then and in each such event the holders of Preferred Stock shall receive, simultaneously with the distribution to the holders of Common Stock, a dividend or other distribution of such securities or other property in an amount equal to the amount of such securities or other property as they would have received if all outstanding shares of Preferred Stock had been converted into Common Stock on the date of such event.

4.8 Adjustment for Merger or Reorganization, etc. Subject to the provisions of Subsection 2.3, if there shall occur any reorganization, recapitalization, reclassification, consolidation or merger involving the Corporation in which the Common Stock (but not the Series A Preferred Stock and/or the Series B Preferred Stock) is converted into or exchanged for securities, cash or other property (other than a transaction covered by Subsections 4.4, 4.6 or 4.7), then, following any such reorganization, recapitalization, reclassification, consolidation or merger, each share of Series A Preferred Stock or Series B Preferred Stock, as applicable, shall thereafter be convertible in lieu of the Common Stock into which it was convertible prior to such event into the kind and amount of securities, cash or other property which a holder of the number of shares of the Common Stock issuable upon conversion of one share of Series A Preferred Stock or Series B Preferred Stock, as applicable, immediately prior to such reorganization, recapitalization, reclassification, consolidation or merger would have been entitled to receive pursuant to such transaction; and, in such case, appropriate adjustment (as determined in good faith by the Board of Directors, including at least one Preferred Director) shall be made in the application of the provisions in this Section 4 with respect to the rights and interests thereafter of the holders of the Series A Preferred Stock or the Series B Preferred Stock, as applicable, to the end that the provisions set forth in this Section 4 (including provisions with respect to changes in and other adjustments of the applicable Preferred Stock Conversion Price) shall thereafter be applicable, as

nearly as reasonably may be, in relation to any securities or other property thereafter deliverable upon the conversion of the applicable series of Preferred Stock.

4.9 Certificate as to Adjustments. Upon the occurrence of each adjustment or readjustment of a Preferred Stock Conversion Price pursuant to this Section 4, the Corporation at its expense shall, as promptly as reasonably practicable but in any event not later than fifteen (15) days thereafter, compute such adjustment or readjustment in accordance with the terms hereof and furnish to each holder of the applicable series of Preferred Stock a certificate setting forth such adjustment or readjustment (including the kind and amount of securities, cash or other property into which such series of Preferred Stock is convertible) and showing in detail the facts upon which such adjustment or readjustment is based. The Corporation shall, as promptly as reasonably practicable after the written request at any time of any holder of Preferred Stock (but in any event not later than fifteen (15) days thereafter), furnish or cause to be furnished to such holder a certificate setting forth (i) the Preferred Stock Conversion Prices then in effect, and (ii) the number of shares of Common Stock and the amount, if any, of other securities, cash or property which then would be received upon the conversion of each series of Preferred Stock.

4.10 Notice of Record Date. In the event:

(a) the Corporation shall take a record of the holders of its Common Stock (or other capital stock or securities at the time issuable upon conversion of the Preferred Stock) for the purpose of entitling or enabling them to receive any dividend or other distribution, or to receive any right to subscribe for or purchase any shares of capital stock of any class or any other securities, or to receive any other security; or

(b) of any capital reorganization of the Corporation, any reclassification of the Common Stock, or any Deemed Liquidation Event; or

(c) of the voluntary or involuntary dissolution, liquidation or winding-up of the Corporation,

then, and in each such case, the Corporation will send or cause to be sent to the holders of the Preferred Stock a notice specifying, as the case may be, (i) the record date for such dividend, distribution or right, and the amount and character of such dividend, distribution or right, or (ii) the effective date on which such reorganization, reclassification, consolidation, merger, transfer, dissolution, liquidation, winding-up or Deemed Liquidation Event is proposed to take place, and the time, if any is to be fixed, as of which the holders of record of Common Stock (or such other capital stock or securities at the time issuable upon the conversion of each series of Preferred Stock) shall be entitled to exchange their shares of Common Stock (or such other capital stock or securities) for securities or other property deliverable upon such reorganization, reclassification, consolidation, merger, transfer, dissolution, liquidation, winding-up or Deemed Liquidation Event, and the amount per share and character of such exchange applicable to the Preferred Stock and the Common Stock. Such notice shall be sent at least ten (10) days prior to the record date or effective date for the event specified in such notice.

5. Mandatory Conversion.

5.1 Trigger Events. Upon either (a) the date and time, or the occurrence of an event, specified by vote or written consent of the holders representing the Required Vote or (b) the closing of the sale of shares of Common Stock to the public in a firm-commitment underwritten public offering pursuant to an effective registration statement under the Securities Act of 1933, as amended (the “**Securities Act**”), provided that such offering results in at least \$45 million of gross proceeds to the Corporation and, following such offering, the Common Stock is listed on the New York Stock Exchange or Nasdaq (the time of such closing or the date and time specified or the time of the event specified in such vote or written consent is referred to herein as the “**Mandatory Conversion Time**”), (i) all outstanding shares of Preferred Stock shall automatically be converted into shares of Common Stock, at the conversion rate in effect immediately prior to the Mandatory Conversion Time and (ii) such shares may not be reissued by the Corporation. Notwithstanding the foregoing, if the holders representing the Required Vote approve such mandatory conversion pursuant to clause (a) of this Section 5.1 in connection with a proposed Deemed Liquidation Event in which the holders of Series B Preferred Stock would receive less than the full Series B Liquidation Amount, then a mandatory conversion pursuant to this Section 5.1 shall also require the consent of the holders representing the Series B Required Vote.

5.2 Procedural Requirements. All holders of record of shares of Preferred Stock shall be sent written notice of the Mandatory Conversion Time and the place designated for mandatory conversion of all such shares of Preferred Stock pursuant to this Section 5. Such notice need not be sent in advance of the occurrence of the Mandatory Conversion Time. Upon receipt of such notice, each holder of shares of Preferred Stock shall surrender his, her or its certificate or certificates for all such shares (or, if such holder alleges that such certificate has been lost, stolen or destroyed, a lost certificate affidavit and agreement reasonably acceptable to the Corporation to indemnify the Corporation against any claim that may be made against the Corporation on account of the alleged loss, theft or destruction of such certificate) to the Corporation at the place designated in such notice, and shall thereafter receive certificates for the number of shares of Common Stock to which such holder is entitled pursuant to this Section 5. At the Mandatory Conversion Time, all outstanding shares of Preferred Stock shall be deemed to have been converted into shares of Common Stock, which shall be deemed to be outstanding of record, and all rights with respect to the Preferred Stock so converted, including the rights, if any, to receive notices and vote (other than as a holder of Common Stock), will terminate, except only the rights of the holders thereof, upon surrender of their certificate or certificates (or lost certificate affidavit and agreement) therefor, to receive the items provided for in the last sentence of this Subsection 5.2. If so required by the Corporation, certificates surrendered for conversion shall be endorsed or accompanied by written instrument or instruments of transfer, in form satisfactory to the Corporation, duly executed by the registered holder or by his, her or its attorney duly authorized in writing. As soon as practicable after the Mandatory Conversion Time and the surrender of the certificate or certificates (or lost certificate affidavit and agreement) for Preferred Stock, the Corporation shall issue and deliver to such holder, or to his, her or its nominees, a certificate or certificates for the number of full shares of Common Stock issuable on such conversion in accordance with the provisions hereof, together with cash as provided in Subsection 4.2 in lieu of any fraction of a share of Common Stock otherwise issuable upon such conversion and the payment of any declared but unpaid dividends on the shares of Preferred Stock converted.

5.3 Effect of Mandatory Conversion. All shares of Preferred Stock shall, from and after the Mandatory Conversion Time, no longer be deemed to be outstanding and,

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notwithstanding the failure of the holder or holders thereof to surrender the certificates for such shares on or prior to such time, all rights with respect to such shares shall immediately cease and terminate at the Mandatory Conversion Time, except only the right of the holders thereof to receive shares of Common Stock in exchange therefor and to receive payment of any dividends accrued and declared but unpaid thereon. Such converted Preferred Stock shall be retired and cancelled and may not be reissued as shares of such series, and the Corporation may thereafter take such appropriate action (without the need for stockholder action) as may be necessary to reduce the authorized number of shares of Preferred Stock accordingly.

6. Redeemed or Otherwise Acquired Shares. Any shares of Preferred Stock that are redeemed or otherwise acquired by the Corporation or any of its subsidiaries shall be automatically and immediately cancelled and retired and shall not be reissued, sold or transferred. Neither the Corporation nor any of its subsidiaries may exercise any voting or other rights granted to the holders of Preferred Stock following redemption.

7. Waiver. Any of the rights, powers, preferences and other terms of the Series A Preferred Stock set forth herein may be waived on behalf of all holders of Series A Preferred Stock by the affirmative written consent or vote of the holders representing the Series A Required Vote. Any of the rights, powers, preferences and other terms of the Series B Preferred Stock set forth herein may be waived on behalf of all holders of Series B Preferred Stock by the affirmative written consent or vote of the holders representing the Series B Required Vote. Any of the rights, powers, preferences and other terms for the benefit of all the Preferred Stock set forth herein may be waived on behalf of all holders of Preferred Stock by the affirmative written consent or vote of the holders representing the Required Vote.

8. Notices. Any notice required or permitted by the provisions of this Article Fourth to be given to a holder of shares of Preferred Stock shall be mailed, postage prepaid, to the post office address last shown on the records of the Corporation, or given by electronic communication in compliance with the provisions of the General Corporation Law, and shall be deemed sent upon such mailing or electronic transmission.

FIFTH: Subject to any additional vote required by the Certificate of Incorporation, in furtherance and not in limitation of the powers conferred by statute, the Board of Directors is expressly authorized to make, repeal, alter, amend and rescind any or all of the Bylaws of the Corporation.

SIXTH: Subject to any additional vote required by the Certificate of Incorporation, the number of directors of the Corporation shall be determined in the manner set forth in the Bylaws of the Corporation.

SEVENTH: Elections of directors need not be by written ballot unless the Bylaws of the Corporation shall so provide.

EIGHTH: Meetings of stockholders may be held within or without the State of Delaware, as the Bylaws of the Corporation may provide. The books of the Corporation may be kept outside the State of Delaware at such place or places as may be designated from time to time by the Board of Directors or in the Bylaws of the Corporation.

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NINTH: To the fullest extent permitted by law, a director of the Corporation shall not be personally liable to the Corporation or its stockholders for monetary damages for breach of fiduciary duty as a director. If the General Corporation Law or any other law of the State of Delaware is amended after approval by the stockholders of this Article Ninth to authorize corporate action further eliminating or limiting the personal liability of directors, then the liability of a director of the Corporation shall be eliminated or limited to the fullest extent permitted by the General Corporation Law as so amended.

Any repeal or modification of the foregoing provisions of this Article Ninth by the stockholders of the Corporation shall not adversely affect any right or protection of a director of the Corporation existing at the time of, or increase the liability of any director of the Corporation with respect to any acts or omissions of such director occurring prior to, such repeal or modification.

TENTH: To the fullest extent permitted by applicable law, the Corporation is authorized to provide indemnification of (and advancement of expenses to) directors, officers and agents of the Corporation (and any other persons to which General Corporation Law permits the Corporation to provide indemnification) through Bylaw provisions, agreements with such agents or other persons, vote of stockholders or disinterested directors or otherwise, in excess of the indemnification and advancement otherwise permitted by Section 145 of the General Corporation Law.

Any amendment, repeal or modification of the foregoing provisions of this Article Tenth shall not adversely affect any right or protection of any director, officer or other agent of the Corporation existing at the time of such amendment, repeal or modification.

ELEVENTH: The Corporation renounces, to the fullest extent permitted by law, any interest or expectancy of the Corporation in, or in being offered an opportunity to participate in, any Excluded Opportunity (as defined below). An “**Excluded Opportunity**” is any matter, transaction or interest that is presented to, or acquired, created or developed by, or which otherwise comes into the possession of, (i) any director of the Corporation who is not an employee of the Corporation or any of its subsidiaries, or (ii) any holder of Preferred Stock or any partner, member, director, stockholder, employee or agent of any such holder, other than someone who is an employee of the Corporation or any of its subsidiaries (collectively, “**Covered Persons**”), unless such matter, transaction or interest is presented to, or acquired, created or developed by, or otherwise comes into the possession of, a Covered Person expressly and solely in such Covered Person’s capacity as a director of the Corporation.

TWELFTH: Unless the Corporation consents in writing to the selection of an alternative forum, the Court of Chancery in the State of Delaware shall be the sole and exclusive forum for any stockholder (including a beneficial owner) to bring (i) any derivative action or proceeding brought on behalf of the Corporation, (ii) any action asserting a claim of breach of fiduciary duty owed by any director, officer or other employee of the Corporation to the Corporation or the Corporation’s stockholders, (iii) any action asserting a claim against the Corporation, its directors, officers or employees arising pursuant to any provision of the Delaware General Corporation Law or the Corporation’s certificate of incorporation or bylaws or (iv) any action asserting a claim against the Corporation, its directors, officers or employees governed by

the internal affairs doctrine, except for, as to each of (i) through (iv) above, any claim as to which the Court of Chancery determines that there is an indispensable party not subject to the jurisdiction of the Court of Chancery (and the indispensable party does not consent to the personal jurisdiction of the Court of Chancery within ten days following such determination), which is vested in the exclusive jurisdiction of a court or forum other than the Court of Chancery, or for which the Court of Chancery does not have subject matter jurisdiction. If any provision or provisions of this Article Twelfth shall be held to be invalid, illegal or unenforceable as applied to any person or entity or circumstance for any reason whatsoever, then, to the fullest extent permitted by law, the validity, legality and enforceability of such provisions in any other circumstance and of the remaining provisions of this Article Twelfth (including, without limitation, each portion of any sentence of this Article Twelfth containing any such provision held to be invalid, illegal or unenforceable that is not itself held to be invalid, illegal or unenforceable) and the application of such provision to other persons or entities and circumstances shall not in any way be affected or impaired thereby.

* * *

3: That the foregoing amendment and restatement was approved by the holders of the requisite number of shares of this corporation in accordance with Section 228 of the General Corporation Law.

4: That this Amended and Restated Certificate of Incorporation, which restates and integrates and further amends the provisions of this corporation's Amended and Restated Certificate of Incorporation, has been duly adopted in accordance with Sections 242 and 245 of the General Corporation Law.

[REMAINDER OF PAGE INTENTIONALLY LEFT BLANK]

IN WITNESS WHEREOF, this Amended and Restated Certificate of Incorporation has been executed by a duly authorized officer of this corporation on this 24th day of August, 2018.

By: /s/ Robert Gould
Name: Robert Gould
Title: President and Chief Executive Officer

[SIGNATURE PAGE TO AMENDED AND RESTATED CERTIFICATE OF INCORPORATION]

**CERTIFICATE OF AMENDMENT
TO THE
AMENDED AND RESTATED CERTIFICATE OF INCORPORATION
OF
FULCRUM THERAPEUTICS, INC.**

Fulcrum Therapeutics, Inc. (the “**Corporation**”), a corporation organized and existing under and by virtue of the General Corporation Law of the State of Delaware (the “**DGCL**”), does hereby certify as follows:

Resolutions were duly adopted by the Board of Directors of the Corporation pursuant to Sections 141(f) and 242 of the DGCL setting forth an amendment to the Amended and Restated Certificate of Incorporation of the Corporation (the “**Certificate of Incorporation**”) and declaring such amendment to be advisable. The stockholders of the Corporation duly approved said proposed amendment by written consent in accordance with Sections 228 and 242 of the DGCL. The resolutions setting forth the amendments are as follows:

RESOLVED: That Certificate of Incorporation is hereby amended by deleting the first paragraph of Article FOURTH in its entirety and by substituting the following in lieu thereof:

“**FOURTH:** The total number of shares of all classes of stock which the Corporation shall have authority to issue is 147,500,000 shares of Common Stock, \$0.001 par value per share (“**Common Stock**”) and 112,500,000 shares of Preferred Stock, \$0.001 par value per share (“**Preferred Stock**”).”

RESOLVED: The Certificate of Incorporation is hereby further amended by deleting the second paragraph of Part B of Article FOURTH in its entirety and by substituting the following in lieu thereof:

“60,000,000 shares of the authorized Preferred Stock of the Corporation are hereby designated “**Series A Preferred Stock**” and 52,500,000 shares of the authorized Preferred Stock of the Corporation are hereby designation “**Series B Preferred Stock**”, each such series with the following rights, preferences, powers, privileges and restrictions, qualifications and limitations. Unless otherwise indicated, references to “Sections” or “Subsections” in this Part B of this Article Fourth refer to sections and subsections of Part B of this Article Fourth.”

[Signature Page Follows]

IN WITNESS WHEREOF, Fulcrum Therapeutics, Inc. has caused this Certificate of Amendment to the Amended and Restated Certificate of Incorporation of the Corporation to be signed and attested by its duly authorized officer, this 7th day of February, 2019.

By: /s/ Robert Gould
Robert Gould, President and Chief Executive Officer

BYLAWS
OF
FULCRUM THERAPEUTICS, INC.
(a Delaware corporation)

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ARTICLE I

STOCKHOLDERS

1.1 Place of Meetings. All meetings of stockholders shall be held at such place as may be designated from time to time by the Board of Directors, the Chairman of the Board, the Chief Executive Officer or the President or, if not so designated, at the principal office of the corporation. The Board of Directors may, in its sole discretion, determine that a meeting shall not be held at any place, but may instead be held solely by means of remote communication in a manner consistent with the General Corporation Law of the State of Delaware.

1.2 Annual Meeting. The annual meeting of stockholders for the election of directors and for the transaction of such other business as may properly be brought before the meeting shall be held on a date and at a time designated by the Board of Directors, the Chairman of the Board, the Chief Executive Officer or the President (which date shall not be a legal holiday in the place where the meeting is to be held).

1.3 Special Meetings. Special meetings of stockholders for any purpose or purposes may be called at any time by only the Board of Directors, the Chairman of the Board, the Chief Executive Officer or the President, and may not be called by any other person or persons. The Board of Directors may postpone or reschedule any previously scheduled special meeting of stockholders. Business transacted at any special meeting of stockholders shall be limited to matters relating to the purpose or purposes stated in the notice of meeting.

1.4 Notice of Meetings. Except as otherwise provided by law, notice of each meeting of stockholders, whether annual or special, shall be given not less than 10 nor more than 60 days before the date of the meeting to each stockholder entitled to vote at such meeting. Without limiting the manner by which notice otherwise may be given to stockholders, any notice shall be effective if given by a form of electronic transmission consented to (in a manner consistent with the General Corporation Law of the State of Delaware) by the stockholder to whom the notice is given. The notices of all meetings shall state the place, if any, date and time of the meeting and the means of remote communications, if any, by which stockholders and proxyholders may be deemed to be present in person and vote at such meeting. The notice of a special meeting shall state, in addition, the purpose or purposes for which the meeting is called. If notice is given by mail, such notice shall be deemed given when deposited in the United States mail, postage prepaid, directed to the stockholder at such stockholder's address as it appears on the records of the corporation. If notice is given by electronic transmission, such notice shall be deemed given at the time specified in Section 232 of the General Corporation Law of the State of Delaware.

1.5 Voting List. The Secretary shall prepare, at least 10 days before every meeting of stockholders, a complete list of the stockholders entitled to vote at the meeting, arranged in alphabetical order, and showing the address of each stockholder and the number of shares registered in the name of each stockholder. Such list shall be open to the examination of any stockholder, for any purpose germane to the meeting, for a period of at least 10 days prior to the meeting: (a) on a reasonably accessible electronic network, provided that the information required to gain access to such list is provided with the notice of the meeting, or (b) during ordinary business hours, at the principal place of business of the corporation. If the meeting is to

be held at a physical location (and not solely by means of remote communication), then the list shall be produced and kept at the time and place of the meeting during the whole time thereof, and may be inspected by any stockholder who is present. If the meeting is to be held solely by means of remote communication, then the list shall also be open to the examination of any stockholder during the whole time of the meeting on a reasonably accessible electronic network, and the information required to access such list shall be provided with the notice of the meeting. The list shall presumptively determine the identity of the stockholders entitled to vote at the meeting and the number of shares held by each of them.

1.6 Quorum. Except as otherwise provided by law, the Certificate of Incorporation or these Bylaws, the holders of a majority in voting power of the shares of the capital stock of the corporation issued and outstanding and entitled to vote at the meeting, present in person, present by means of remote communication in a manner, if any, authorized by the Board of Directors in its sole discretion, or represented by proxy, shall constitute a quorum for the transaction of business; provided, however, that where a separate vote by a class or classes or series of capital stock is required by law or the Certificate of Incorporation, the holders of a majority in voting power of the shares of such class or classes or series of the capital stock of the corporation issued and outstanding and entitled to vote on such matter, present in person, present by means of remote communication in a manner, if any, authorized by the Board of Directors in its sole discretion, or represented by proxy, shall constitute a quorum entitled to take action with respect to the vote on such matter. A quorum, once established at a meeting, shall not be broken by the withdrawal of enough votes to leave less than a quorum.

1.7 Adjournments. Any meeting of stockholders may be adjourned from time to time to any other time and to any other place at which a meeting of stockholders may be held under these Bylaws by the chairman of the meeting or by the stockholders present or represented at the meeting and entitled to vote, although less than a quorum. It shall not be necessary to notify any stockholder of any adjournment of less than 30 days if the time and place, if any, of the adjourned meeting, and the means of remote communication, if any, by which stockholders and proxyholders may be deemed to be present in person and vote at such adjourned meeting, are announced at the meeting at which adjournment is taken, unless after the adjournment a new record date is fixed for the adjourned meeting. At the adjourned meeting, the corporation may transact any business which might have been transacted at the original meeting.

1.8 Voting and Proxies. Each stockholder shall have one vote for each share of stock entitled to vote held of record by such stockholder and a proportionate vote for each fractional share so held, unless otherwise provided by law or the Certificate of Incorporation. Each stockholder of record entitled to vote at a meeting of stockholders, or to express consent or dissent to corporate action without a meeting, may vote or express such consent or dissent in person (including by means of remote communications, if any, by which stockholders may be deemed to be present in person and vote at such meeting) or may authorize another person or persons to vote or act for such stockholder by a proxy executed or transmitted in a manner permitted by the General Corporation Law of the State of Delaware by the stockholder or such stockholder's authorized agent and delivered (including by electronic transmission) to the Secretary of the corporation. No such proxy shall be voted or acted upon after three years from the date of its execution, unless the proxy expressly provides for a longer period.

1.9 Action at Meeting. When a quorum is present at any meeting, any matter other than the election of directors to be voted upon by the stockholders at such meeting shall be decided by the vote of the holders of shares of stock having a majority in voting power of the votes cast by the holders of all of the shares of stock present or represented at the meeting and voting affirmatively or negatively on such matter (or if there are two or more classes or series of stock entitled to vote as separate classes, then in the case of each such class or series, the holders of a majority in voting power of the shares of stock of that class or series present or represented at the meeting and voting affirmatively or negatively on such matter), except when a different vote is required by law, the Certificate of Incorporation or these Bylaws. When a quorum is present at any meeting, any election by stockholders of directors shall be determined by a plurality of the votes cast by the stockholders entitled to vote on the election.

1.10 Conduct of Meetings.

(a) Chairman of Meeting. Meetings of stockholders shall be presided over by the Chairman of the Board, if any, or in the Chairman's absence by the Vice Chairman of the Board, if any, or in the Vice Chairman's absence by the Chief Executive Officer, or in the Chief Executive Officer's absence, by the President, or in the President's absence by a Vice President, or in the absence of all of the foregoing persons by a chairman designated by the Board of Directors, or in the absence of such designation by a chairman chosen by vote of the stockholders at the meeting. The Secretary shall act as secretary of the meeting, but in the Secretary's absence the chairman of the meeting may appoint any person to act as secretary of the meeting.

(b) Rules, Regulations and Procedures. The Board of Directors may adopt by resolution such rules, regulations and procedures for the conduct of any meeting of stockholders of the corporation as it shall deem appropriate including, without limitation, such guidelines and procedures as it may deem appropriate regarding the participation by means of remote communication of stockholders and proxyholders not physically present at a meeting. Except to the extent inconsistent with such rules, regulations and procedures as adopted by the Board of Directors, the chairman of any meeting of stockholders shall have the right and authority to prescribe such rules, regulations and procedures and to do all such acts as, in the judgment of such chairman, are appropriate for the proper conduct of the meeting. Such rules, regulations or procedures, whether adopted by the Board of Directors or prescribed by the chairman of the meeting, may include, without limitation, the following: (i) the establishment of an agenda or order of business for the meeting; (ii) rules and procedures for maintaining order at the meeting and the safety of those present; (iii) limitations on attendance at or participation in the meeting to stockholders of record of the corporation, their duly authorized and constituted proxies or such other persons as shall be determined; (iv) restrictions on entry to the meeting after the time fixed for the commencement thereof; and (v) limitations on the time allotted to questions or comments by participants. Unless and to the extent determined by the Board of Directors or the chairman of the meeting, meetings of stockholders shall not be required to be held in accordance with the rules of parliamentary procedure.

1.11 Action without Meeting.

(a) Taking of Action by Consent. Any action required or permitted to be taken at any annual or special meeting of stockholders of the corporation may be taken without a meeting, without prior notice and without a vote, if a consent in writing, setting forth the action so taken, is signed by the holders of outstanding stock having not less than the minimum number of votes that would be necessary to authorize or take such action at a meeting at which all shares entitled to vote on such action were present and voted. Except as otherwise provided by the Certificate of Incorporation, stockholders may act by written consent to elect directors; provided, however, that, if such consent is less than unanimous, such action by written consent may be in lieu of holding an annual meeting only if all of the directorships to which directors could be elected at an annual meeting held at the effective time of such action are vacant and are filled by such action.

(b) Electronic Transmission of Consents. A telegram, cablegram or other electronic transmission consenting to an action to be taken and transmitted by a stockholder or proxyholder, or by a person or persons authorized to act for a stockholder or proxyholder, shall be deemed to be written, signed and dated for the purposes of this section, provided that any such telegram, cablegram or other electronic transmission sets forth or is delivered with information from which the corporation can determine (i) that the telegram, cablegram or other electronic transmission was transmitted by the stockholder or proxyholder or by a person or persons authorized to act for the stockholder or proxyholder and (ii) the date on which such stockholder or proxyholder or authorized person or persons transmitted such telegram, cablegram or electronic transmission. The date on which such telegram, cablegram or electronic transmission is transmitted shall be deemed to be the date on which such consent was signed. No consent given by telegram, cablegram or other electronic transmission shall be deemed to have been delivered until such consent is reproduced in paper form and until such paper form shall be delivered to the corporation by delivery to its registered office in the State of Delaware, its principal place of business or an officer or agent of the corporation having custody of the book in which proceedings of meetings of stockholders are recorded. Delivery made to a corporation's registered office shall be made by hand or by certified or registered mail, return receipt requested. Notwithstanding the foregoing limitations on delivery, consents given by telegram, cablegram or other electronic transmission may be otherwise delivered to the principal place of business of the corporation or to an officer or agent of the corporation having custody of the book in which proceedings of meetings of stockholders are recorded if, to the extent and in the manner provided by resolution of the Board of Directors. Any copy, facsimile or other reliable reproduction of a consent in writing may be substituted or used in lieu of the original writing for any and all purposes for which the original writing could be used, provided that such copy, facsimile or other reproduction shall be a complete reproduction of the entire original writing.

(c) Notice of Taking of Corporate Action. Prompt notice of the taking of corporate action without a meeting by less than unanimous written consent shall be given to those stockholders who have not consented in writing and who, if the action had been taken at a meeting, would have been entitled to notice of the meeting if the record date for such meeting had been the date that written consents signed by a sufficient number of holders to take the action were delivered to the corporation.

ARTICLE II

DIRECTORS

2.1 General Powers. The business and affairs of the corporation shall be managed by or under the direction of a Board of Directors, who may exercise all of the powers of the corporation except as otherwise provided by law or the Certificate of Incorporation.

2.2 Number, Election and Qualification. Subject to the rights of holders of any series of Preferred Stock to elect directors, the number of directors of the corporation shall be established from time to time by the stockholders or the Board of Directors. The directors shall be elected at the annual meeting of stockholders by such stockholders as have the right to vote on such election. Election of directors need not be by written ballot. Directors need not be stockholders of the corporation.

2.3 Chairman of the Board; Vice Chairman of the Board. The Board of Directors may appoint from its members a Chairman of the Board and a Vice Chairman of the Board, neither of whom need be an employee or officer of the corporation. If the Board of Directors appoints a Chairman of the Board, such Chairman shall perform such duties and possess such powers as are assigned by the Board of Directors and, if the Chairman of the Board is also designated as the corporation's Chief Executive Officer, shall have the powers and duties of the Chief Executive Officer prescribed in Section 3.7 of these Bylaws. If the Board of Directors appoints a Vice Chairman of the Board, such Vice Chairman shall perform such duties and possess such powers as are assigned by the Board of Directors. Unless otherwise provided by the Board of Directors, the Chairman of the Board or, in the Chairman's absence, the Vice Chairman of the Board, if any, shall preside at all meetings of the Board of Directors.

2.4 Tenure. Each director shall hold office until the next annual meeting of stockholders and until a successor is elected and qualified, or until such director's earlier death, resignation or removal.

2.5 Quorum. The greater of (a) a majority of the directors at any time in office and (b) one-third of the number of directors fixed pursuant to Section 2.2 of these Bylaws shall constitute a quorum of the Board of Directors. If at any meeting of the Board of Directors there shall be less than such a quorum, a majority of the directors present may adjourn the meeting from time to time without further notice other than announcement at the meeting, until a quorum shall be present.

2.6 Action at Meeting. Every act or decision done or made by a majority of the directors present at a meeting of the Board of Directors duly held at which a quorum is present shall be regarded as the act of the Board of Directors, unless a greater number is required by law or by the Certificate of Incorporation.

2.7 Removal. Except as otherwise provided by the General Corporation Law of the State of Delaware, any one or more or all of the directors of the corporation may be removed, with or without cause, by the holders of a majority of the shares then entitled to vote at an election of directors, except that the directors elected by the holders of a particular class or series

of stock may be removed without cause only by vote of the holders of a majority of the outstanding shares of such class or series.

2.8 Vacancies. Subject to the rights of holders of any series of Preferred Stock to elect directors, unless and until filled by the stockholders, any vacancy or newly-created directorship on the Board of Directors, however occurring, may be filled by vote of a majority of the directors then in office, although less than a quorum, or by a sole remaining director. A director elected to fill a vacancy shall be elected for the unexpired term of such director's predecessor in office, and a director chosen to fill a position resulting from a newly-created directorship shall hold office until the next annual meeting of stockholders and until a successor is elected and qualified, or until such director's earlier death, resignation or removal.

2.9 Resignation. Any director may resign by delivering a resignation in writing or by electronic transmission to the corporation at its principal office or to the Chairman of the Board, the Chief Executive Officer, the President or the Secretary. Such resignation shall be effective upon delivery unless it is specified to be effective at some later time or upon the happening of some later event.

2.10 Regular Meetings. Regular meetings of the Board of Directors may be held without notice at such time and place as shall be determined from time to time by the Board of Directors; provided that any director who is absent when such a determination is made shall be given notice of the determination. A regular meeting of the Board of Directors may be held without notice immediately after and at the same place as the annual meeting of stockholders.

2.11 Special Meetings. Special meetings of the Board of Directors may be held at any time and place designated in a call by the Chairman of the Board, the Chief Executive Officer, the President, two or more directors, or by one director in the event that there is only a single director in office.

2.12 Notice of Special Meetings. Notice of the date, place, if any, and time of any special meeting of directors shall be given to each director by the Secretary or by the officer or one of the directors calling the meeting. Notice shall be duly given to each director (a) in person or by telephone at least 24 hours in advance of the meeting, (b) by sending written notice by reputable overnight courier, telecopy, facsimile or electronic transmission, or delivering written notice by hand, to such director's last known business, home or electronic transmission address at least 48 hours in advance of the meeting, or (c) by sending written notice by first-class mail to such director's last known business or home address at least 72 hours in advance of the meeting. A notice or waiver of notice of a meeting of the Board of Directors need not specify the purposes of the meeting.

2.13 Meetings by Conference Communications Equipment. Directors may participate in meetings of the Board of Directors or any committee thereof by means of conference telephone or other communications equipment by means of which all persons participating in the meeting can hear each other, and participation by such means shall constitute presence in person at such meeting.

2.14 Action by Consent. Any action required or permitted to be taken at any meeting of the Board of Directors or of any committee thereof may be taken without a meeting, if all members of the Board of Directors or committee, as the case may be, consent to the action in writing or by electronic transmission, and the written consents or electronic transmissions are filed with the minutes of proceedings of the Board of Directors or committee. Such filing shall be in paper form if the minutes are maintained in paper form and shall be in electronic form if the minutes are maintained in electronic form.

2.15 Committees. The Board of Directors may designate one or more committees, each committee to consist of one or more of the directors of the corporation with such lawfully delegable powers and duties as the Board of Directors thereby confers, to serve at the pleasure of the Board of Directors. The Board of Directors may designate one or more directors as alternate members of any committee, who may replace any absent or disqualified member at any meeting of the committee. In the absence or disqualification of a member of a committee, the member or members of the committee present at any meeting and not disqualified from voting, whether or not such member or members constitute a quorum, may unanimously appoint another member of the Board of Directors to act at the meeting in the place of any such absent or disqualified member. Any such committee, to the extent provided in the resolution of the Board of Directors and subject to the provisions of law, shall have and may exercise all the powers and authority of the Board of Directors in the management of the business and affairs of the corporation and may authorize the seal of the corporation to be affixed to all papers which may require it. Each such committee shall keep minutes and make such reports as the Board of Directors may from time to time request. Except as the Board of Directors may otherwise determine, any committee may make rules for the conduct of its business, but unless otherwise provided by the directors or in such rules, its business shall be conducted as nearly as possible in the same manner as is provided in these Bylaws for the Board of Directors. Except as otherwise provided in the Certificate of Incorporation, these Bylaws, or the resolution of the Board of Directors designating the committee, a committee may create one or more subcommittees, each subcommittee to consist of one or more members of the committee, and delegate to a subcommittee any or all of the powers and authority of the committee.

2.16 Compensation of Directors. Directors may be paid such compensation for their services and such reimbursement for expenses of attendance at meetings as the Board of Directors may from time to time determine. No such payment shall preclude any director from serving the corporation or any of its parent or subsidiary entities in any other capacity and receiving compensation for such service.

ARTICLE III

OFFICERS

3.1 Titles. The officers of the corporation shall consist of a Chief Executive Officer, a President, a Secretary, a Treasurer and such other officers with such other titles as the Board of Directors shall determine, including one or more Vice Presidents, Assistant Treasurers and Assistant Secretaries. The Board of Directors may appoint such other officers as it may deem appropriate.

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3.2 Election. The Chief Executive Officer, President, Treasurer and Secretary shall be elected annually by the Board of Directors at its first meeting following the annual meeting of stockholders. Other officers may be appointed by the Board of Directors at such meeting or at any other meeting.

3.3 Qualification. No officer need be a stockholder. Any two or more offices may be held by the same person.

3.4 Tenure. Except as otherwise provided by law, by the Certificate of Incorporation or by these Bylaws, each officer shall hold office until such officer's successor is elected and qualified, unless a different term is specified in the resolution electing or appointing such officer, or until such officer's earlier death, resignation or removal.

3.5 Resignation and Removal. Any officer may resign by delivering a written resignation to the corporation at its principal office or to the Chief Executive Officer, the President or the Secretary. Such resignation shall be effective upon receipt unless it is specified to be effective at some later time or upon the happening of some later event. Any officer may be removed at any time, with or without cause, by vote of a majority of the directors then in office. Except as the Board of Directors may otherwise determine, no officer who resigns or is removed shall have any right to any compensation as an officer for any period following such officer's resignation or removal, or any right to damages on account of such removal, whether such officer's compensation be by the month or by the year or otherwise, unless such compensation is expressly provided for in a duly authorized written agreement with the corporation.

3.6 Vacancies. The Board of Directors may fill any vacancy occurring in any office for any reason and may, in its discretion, leave unfilled for such period as it may determine any offices other than those of Chief Executive Officer, President, Treasurer and Secretary. Each such successor shall hold office for the unexpired term of such officer's predecessor and until a successor is elected and qualified, or until such officer's earlier death, resignation or removal.

3.7 President; Chief Executive Officer. Unless the Board of Directors has designated another person as the corporation's Chief Executive Officer, the President shall be the Chief Executive Officer of the corporation. The Chief Executive Officer shall have general charge and supervision of the business of the corporation subject to the direction of the Board of Directors, and shall perform all duties and have all powers that are commonly incident to the office of chief executive or that are delegated to such officer by the Board of Directors. The President shall perform such other duties and shall have such other powers as the Board of Directors or the Chief Executive Officer (if the President is not the Chief Executive Officer) may from time to time prescribe. In the event of the absence, inability or refusal to act of the Chief Executive Officer or the President (if the President is not the Chief Executive Officer), the Vice President (or if there shall be more than one, the Vice Presidents in the order determined by the Board of Directors) shall perform the duties of the Chief Executive Officer and when so performing such duties shall have all the powers of and be subject to all the restrictions upon the Chief Executive Officer.

3.8 Vice Presidents. Each Vice President shall perform such duties and possess such powers as the Board of Directors or the Chief Executive Officer may from time to time

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prescribe. The Board of Directors may assign to any Vice President the title of Executive Vice President, Senior Vice President or any other title selected by the Board of Directors.

3.9 Secretary and Assistant Secretaries. The Secretary shall perform such duties and shall have such powers as the Board of Directors or the Chief Executive Officer may from time to time prescribe. In addition, the Secretary shall perform such duties and have such powers as are incident to the office of the secretary, including without limitation the duty and power to give notices of all meetings of stockholders and special meetings of the Board of Directors, to attend all meetings of stockholders and the Board of Directors and keep a record of the proceedings, to maintain a stock ledger and prepare lists of stockholders and their addresses as required, to be custodian of corporate records and the corporate seal and to affix and attest to the same on documents.

Any Assistant Secretary shall perform such duties and possess such powers as the Board of Directors, the Chief Executive Officer or the Secretary may from time to time prescribe. In the event of the absence, inability or refusal to act of the Secretary, the Assistant Secretary (or if there shall be more than one, the Assistant Secretaries in the order determined by the Board of Directors) shall perform the duties and exercise the powers of the Secretary.

In the absence of the Secretary or any Assistant Secretary at any meeting of stockholders or directors, the chairman of the meeting shall designate a temporary secretary to keep a record of the meeting.

3.10 Treasurer and Assistant Treasurers. The Treasurer shall perform such duties and shall have such powers as may from time to time be assigned by the Board of Directors or the Chief Executive Officer. In addition, the Treasurer shall perform such duties and have such powers as are incident to the office of treasurer, including without limitation the duty and power to keep and be responsible for all funds and securities of the corporation, to deposit funds of the corporation in depositories selected in accordance with these Bylaws, to disburse such funds as ordered by the Board of Directors, to make proper accounts of such funds, and to render as required by the Board of Directors statements of all such transactions and of the financial condition of the corporation.

The Assistant Treasurers shall perform such duties and possess such powers as the Board of Directors, the Chief Executive Officer or the Treasurer may from time to time prescribe. In the event of the absence, inability or refusal to act of the Treasurer, the Assistant Treasurer (or if there shall be more than one, the Assistant Treasurers in the order determined by the Board of Directors) shall perform the duties and exercise the powers of the Treasurer.

3.11 Salaries. Officers of the corporation shall be entitled to such salaries, compensation or reimbursement as shall be fixed or allowed from time to time by the Board of Directors.

3.12 Delegation of Authority. The Board of Directors may from time to time delegate the powers or duties of any officer to any other officer or agent, notwithstanding any provision hereof.

ARTICLE IV

CAPITAL STOCK

4.1 Issuance of Stock. Subject to the provisions of the Certificate of Incorporation, the whole or any part of any unissued balance of the authorized capital stock of the corporation or the whole or any part of any shares of the authorized capital stock of the corporation held in the corporation's treasury may be issued, sold, transferred or otherwise disposed of by vote of the Board of Directors in such manner, for such lawful consideration and on such terms as the Board of Directors may determine.

4.2 Stock Certificates; Uncertificated Shares. The shares of the corporation shall be represented by certificates, provided that the Board of Directors may provide by resolution or resolutions that some or all of any or all classes or series of the corporation's stock shall be uncertificated shares. Every holder of stock of the corporation represented by certificates shall be entitled to have a certificate, in such form as may be prescribed by law and by the Board of Directors, representing the number of shares held by such holder registered in certificate form. Each such certificate shall be signed in a manner that complies with Section 158 of the General Corporation Law of the State of Delaware.

Each certificate for shares of stock which are subject to any restriction on transfer pursuant to the Certificate of Incorporation, these Bylaws, applicable securities laws or any agreement among any number of stockholders or among such holders and the corporation shall have conspicuously noted on the face or back of the certificate either the full text of the restriction or a statement of the existence of such restriction.

If the corporation shall be authorized to issue more than one class of stock or more than one series of any class, the powers, designations, preferences and relative, participating, optional or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights shall be set forth in full or summarized on the face or back of each certificate representing shares of such class or series of stock, provided that in lieu of the foregoing requirements there may be set forth on the face or back of each certificate representing shares of such class or series of stock a statement that the corporation will furnish without charge to each stockholder who so requests a copy of the full text of the powers, designations, preferences and relative, participating, optional or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights.

Within a reasonable time after the issuance or transfer of uncertificated shares, the corporation shall send to the registered owner thereof a written notice containing the information required to be set forth or stated on certificates pursuant to Sections 151, 202(a) or 218(a) of the General Corporation Law of the State of Delaware or, with respect to Section 151 of the General Corporation Law of the State of Delaware, a statement that the corporation will furnish without charge to each stockholder who so requests the powers, designations, preferences and relative participating, optional or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights.

4.3 Transfers. Shares of stock of the corporation shall be transferable in the manner prescribed by law and in these Bylaws. Transfers of shares of stock of the corporation shall be made only on the books of the corporation or by transfer agents designated to transfer shares of stock of the corporation. Subject to applicable law, shares of stock represented by certificates shall be transferred only on the books of the corporation by the surrender to the corporation or its transfer agent of the certificate representing such shares properly endorsed or accompanied by a written assignment or power of attorney properly executed, and with such proof of authority or the authenticity of signature as the corporation or its transfer agent may reasonably require. Except as may be otherwise required by law, by the Certificate of Incorporation or by these Bylaws, the corporation shall be entitled to treat the record holder of stock as shown on its books as the owner of such stock for all purposes, including the payment of dividends and the right to vote with respect to such stock, regardless of any transfer, pledge or other disposition of such stock until the shares have been transferred on the books of the corporation in accordance with the requirements of these Bylaws.

4.4 Lost, Stolen or Destroyed Certificates. The corporation may issue a new certificate of stock in place of any previously issued certificate alleged to have been lost, stolen or destroyed, upon such terms and conditions as the Board of Directors may prescribe, including the presentation of reasonable evidence of such loss, theft or destruction and the giving of such indemnity and posting of such bond as the Board of Directors may require for the protection of the corporation or any transfer agent or registrar.

4.5 Record Date. The Board of Directors may fix in advance a date as a record date for the determination of the stockholders entitled to notice of or to vote at any meeting of stockholders or to express consent (or dissent) to corporate action without a meeting, or entitled to receive payment of any dividend or other distribution or allotment of any rights in respect of any change, conversion or exchange of stock, or for the purpose of any other lawful action. Such record date shall not precede the date on which the resolution fixing the record date is adopted, and such record date shall not be more than 60 nor less than 10 days before the date of such meeting, nor more than 10 days after the date of adoption of a record date for a consent without a meeting, nor more than 60 days prior to any other action to which such record date relates.

If no record date is fixed, the record date for determining stockholders entitled to notice of or to vote at a meeting of stockholders shall be at the close of business on the day before the day on which notice is given, or, if notice is waived, at the close of business on the day before the day on which the meeting is held. If no record date is fixed, the record date for determining stockholders entitled to express consent to corporate action without a meeting, when no prior action by the Board of Directors is necessary, shall be the day on which the first consent is properly delivered to the corporation. If no record date is fixed, the record date for determining stockholders for any other purpose shall be at the close of business on the day on which the Board of Directors adopts the resolution relating to such purpose.

A determination of stockholders of record entitled to notice of or to vote at a meeting of stockholders shall apply to any adjournment of the meeting; provided, however, that the Board of Directors may fix a new record date for the adjourned meeting.

4.6 Regulations. The issue, transfer, conversion and registration of shares of stock of the corporation shall be governed by such other regulations as the Board of Directors may establish.

ARTICLE V

GENERAL PROVISIONS

5.1 Fiscal Year. Except as from time to time otherwise designated by the Board of Directors, the fiscal year of the corporation shall begin on the first day of January of each year and end on the last day of December in each year.

5.2 Corporate Seal. The corporate seal shall be in such form as shall be approved by the Board of Directors.

5.3 Waiver of Notice. Whenever notice is required to be given by law, by the Certificate of Incorporation or by these Bylaws, a written waiver, signed by the person entitled to notice, or a waiver by electronic transmission by the person entitled to notice, whether before, at or after the time of the event for which notice is to be given, shall be deemed equivalent to notice required to be given to such person. Neither the business nor the purpose of any meeting need be specified in any such waiver. Attendance of a person at a meeting shall constitute a waiver of notice of such meeting, except when the person attends a meeting for the express purpose of objecting at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened.

5.4 Voting of Securities. Except as the Board of Directors may otherwise designate, the Chief Executive Officer, the President or the Treasurer may waive notice of, vote, or appoint any person or persons to vote, on behalf of the corporation at, and act as, or appoint any person or persons to act as, proxy or attorney-in-fact for this corporation (with or without power of substitution) at, any meeting of stockholders or securityholders of any other entity, the securities of which may be held by this corporation.

5.5 Evidence of Authority. A certificate by the Secretary, or an Assistant Secretary, or a temporary Secretary, as to any action taken by the stockholders, directors, a committee or any officer or representative of the corporation shall as to all persons who rely on the certificate in good faith be conclusive evidence of such action.

5.6 Certificate of Incorporation. All references in these Bylaws to the Certificate of Incorporation shall be deemed to refer to the Certificate of Incorporation of the corporation, as amended and in effect from time to time.

5.7 Severability. Any determination that any provision of these Bylaws is for any reason inapplicable, illegal or ineffective shall not affect or invalidate any other provision of these Bylaws.

5.8 Pronouns. All pronouns used in these Bylaws shall be deemed to refer to the masculine, feminine or neuter, singular or plural, as the identity of the person or persons may require.

ARTICLE VI

AMENDMENTS

6.1 By the Board of Directors. These Bylaws may be altered, amended or repealed, in whole or in part, or new bylaws may be adopted by the Board of Directors.

6.2 By the Stockholders. These Bylaws may be altered, amended or repealed, in whole or in part, or new bylaws may be adopted by the affirmative vote of the holders of a majority of the shares of the capital stock of the corporation issued and outstanding and entitled to vote at any annual meeting of stockholders, or at any special meeting of stockholders, provided notice of such alteration, amendment, repeal or adoption of new bylaws shall have been stated in the notice of such special meeting.

RESTATED CERTIFICATE OF INCORPORATION

OF

FULCRUM THERAPEUTICS, INC.

(originally incorporated on August 18, 2015)

FIRST: The name of the Corporation is Fulcrum Therapeutics, Inc.

SECOND: The address of the Corporation's registered office in the State of Delaware is Corporation Trust Center, 1209 Orange Street, in the City of Wilmington, County of New Castle, 19801. The name of its registered agent at that address is The Corporation Trust Company.

THIRD: The nature of the business or purposes to be conducted or promoted by the Corporation is to engage in any lawful act or activity for which corporations may be organized under the General Corporation Law of the State of Delaware.

FOURTH: The total number of shares of all classes of stock that the Corporation shall have authority to issue is 205,000,000 shares, consisting of (i) 200,000,000 shares of Common Stock, \$0.001 par value per share ("Common Stock"), and (ii) 5,000,000 shares of Preferred Stock, \$0.001 par value per share ("Preferred Stock").

The following is a statement of the designations and the powers, privileges and rights, and the qualifications, limitations or restrictions thereof in respect of each class of capital stock of the Corporation.

A COMMON STOCK.

1. General. The voting, dividend and liquidation rights of the holders of the Common Stock are subject to and qualified by the rights of the holders of the Preferred Stock of any series as may be designated by the Board of Directors upon any issuance of the Preferred Stock of any series.

2. Voting. The holders of the Common Stock shall have voting rights at all meetings of stockholders, each such holder being entitled to one vote for each share thereof held by such holder; provided, however, that, except as otherwise required by law, holders of Common Stock shall not be entitled to vote on any amendment to this Certificate of Incorporation (which, as used herein, shall mean the certificate of incorporation of the Corporation, as amended from time to time, including the terms of any certificate of designations of any series of Preferred Stock) that relates solely to the terms of one or more outstanding series of Preferred Stock if the holders of such affected series are entitled, either separately or together as a class with the holders of one or more other such series, to vote thereon pursuant to this Certificate of Incorporation or the General Corporation Law of the State of Delaware. There shall be no cumulative voting.

The number of authorized shares of Common Stock may be increased or decreased (but not below the number of shares thereof then outstanding) by the affirmative vote of the holders

of a majority of the stock of the Corporation entitled to vote, irrespective of the provisions of Section 242(b)(2) of the General Corporation Law of the State of Delaware.

3. Dividends. Dividends may be declared and paid on the Common Stock from funds lawfully available therefor if, as and when determined by the Board of Directors and subject to any preferential dividend or other rights of any then outstanding Preferred Stock.

4. Liquidation. Upon the dissolution, liquidation or winding up of the Corporation, whether voluntary or involuntary, holders of Common Stock will be entitled to receive all assets of the Corporation available for distribution to its stockholders, subject to any preferential or other rights of any then outstanding Preferred Stock.

B PREFERRED STOCK.

Preferred Stock may be issued from time to time in one or more series, each of such series to have such terms as stated or expressed herein and in the resolution or resolutions providing for the issue of such series adopted by the Board of Directors of the Corporation as hereinafter provided. Any shares of Preferred Stock that may be redeemed, purchased or acquired by the Corporation may be reissued except as otherwise provided by law.

Authority is hereby expressly granted to the Board of Directors from time to time to issue the Preferred Stock in one or more series, and in connection with the creation of any such series, by adopting a resolution or resolutions providing for the issuance of the shares thereof and by filing a certificate of designations relating thereto in accordance with the General Corporation Law of the State of Delaware, to determine and fix the number of shares of such series and such voting powers, full or limited, or no voting powers, and such designations, preferences and relative, participating, optional or other special rights, and qualifications, limitations or restrictions thereof, including dividend rights, conversion rights, redemption privileges and liquidation preferences, as shall be stated and expressed in such resolutions, all to the full extent now or hereafter permitted by the General Corporation Law of the State of Delaware. Without limiting the generality of the foregoing, the resolutions providing for issuance of any series of Preferred Stock may provide that such series shall be superior or rank equally or be junior to any other series of Preferred Stock to the extent permitted by law. The powers, preferences and relative, participating, optional and other special rights of each series of Preferred Stock, and the qualifications, limitations or restrictions thereof, if any, may differ from those of any and all other series at any time outstanding.

The number of authorized shares of Preferred Stock may be increased or decreased (but not below the number of shares then outstanding) by the affirmative vote of the holders of a majority of the voting power of the capital stock of the Corporation entitled to vote thereon, voting as a single class, irrespective of the provisions of Section 242(b)(2) of the General Corporation Law of the State of Delaware.

FIFTH: Except as otherwise provided herein, the Corporation reserves the right to amend, alter, change or repeal any provision contained in this Certificate of Incorporation, in the manner now or hereafter prescribed by statute and this Certificate of Incorporation, and all rights conferred upon stockholders herein are granted subject to this reservation.

SIXTH: In furtherance and not in limitation of the powers conferred upon it by the General Corporation Law of the State of Delaware, and subject to the terms of any series of Preferred Stock, the Board of Directors shall have the power to adopt, amend, alter or repeal the Bylaws of the Corporation by the affirmative vote of a majority of the directors present at any regular or special meeting of the Board of Directors at which a quorum is present. The stockholders may not adopt, amend, alter or repeal the Bylaws of the Corporation, or adopt any provision inconsistent therewith, unless such action is approved, in addition to any other vote required by this Certificate of Incorporation, by the affirmative vote of the holders of at least seventy-five percent (75%) of the votes that all the stockholders would be entitled to cast in an election of directors or class of directors. Notwithstanding any other provisions of law, this Certificate of Incorporation or the Bylaws of the Corporation, and notwithstanding the fact that a lesser percentage may be specified by law, the affirmative vote of the holders of at least seventy-five percent (75%) of the votes that all the stockholders would be entitled to cast in an election of directors or class of directors shall be required to amend or repeal, or to adopt any provision inconsistent with, this Article SIXTH.

SEVENTH: Except to the extent that the General Corporation Law of the State of Delaware prohibits the elimination or limitation of liability of directors for breaches of fiduciary duty, no director of the Corporation shall be personally liable to the Corporation or its stockholders for monetary damages for any breach of fiduciary duty as a director, notwithstanding any provision of law imposing such liability. No amendment to or repeal of this provision shall apply to or have any effect on the liability or alleged liability of any director of the Corporation for or with respect to any acts or omissions of such director occurring prior to such amendment or repeal. If the General Corporation Law of the State of Delaware is amended to permit further elimination or limitation of the personal liability of directors, then the liability of a director of the Corporation shall be eliminated or limited to the fullest extent permitted by the General Corporation Law of the State of Delaware as so amended.

EIGHTH: The Corporation shall provide indemnification and advancement of expenses as follows:

1. Actions, Suits and Proceedings Other than by or in the Right of the Corporation. The Corporation shall indemnify each person who was or is a party or threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of the Corporation) by reason of the fact that he or she is or was, or has agreed to become, a director or officer of the Corporation, or is or was serving, or has agreed to serve, at the request of the Corporation, as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan) (all such persons being referred to hereafter as an "Indemnitee"), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees), liabilities, losses, judgments, fines (including excise taxes and penalties arising under the Employee Retirement Income Security Act of 1974), and amounts paid in settlement actually and reasonably incurred by or on behalf of Indemnitee in connection with such action, suit or proceeding and any appeal therefrom, if Indemnitee acted in good faith and in a manner which Indemnitee reasonably believed to be in, or not opposed to, the best interests of the Corporation, and, with respect to any criminal action or proceeding, had no reasonable cause to believe his or

her conduct was unlawful. The termination of any action, suit or proceeding by judgment, order, settlement, conviction or upon a plea of nolo contendere or its equivalent, shall not, of itself, create a presumption that Indemnitee did not act in good faith and in a manner which Indemnitee reasonably believed to be in, or not opposed to, the best interests of the Corporation, and, with respect to any criminal action or proceeding, had reasonable cause to believe that his or her conduct was unlawful.

2. Actions or Suits by or in the Right of the Corporation. The Corporation shall indemnify any Indemnitee who was or is a party to or threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the Corporation to procure a judgment in its favor by reason of the fact that Indemnitee is or was, or has agreed to become, a director or officer of the Corporation, or is or was serving, or has agreed to serve, at the request of the Corporation, as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees) and, to the extent permitted by law, amounts paid in settlement actually and reasonably incurred by or on behalf of Indemnitee in connection with such action, suit or proceeding and any appeal therefrom, if Indemnitee acted in good faith and in a manner which Indemnitee reasonably believed to be in, or not opposed to, the best interests of the Corporation, except that no indemnification shall be made under this Section 2 in respect of any claim, issue or matter as to which Indemnitee shall have been adjudged to be liable to the Corporation, unless, and only to the extent, that the Court of Chancery of Delaware or the court in which such action or suit was brought shall determine upon application that, despite the adjudication of such liability but in view of all the circumstances of the case, Indemnitee is fairly and reasonably entitled to indemnity for such expenses (including attorneys' fees) which the Court of Chancery of Delaware or such other court shall deem proper.

3. Indemnification for Expenses of Successful Party. Notwithstanding any other provisions of this Article EIGHTH, to the extent that an Indemnitee has been successful, on the merits or otherwise, in defense of any action, suit or proceeding referred to in Sections 1 and 2 of this Article EIGHTH, or in defense of any claim, issue or matter therein, or on appeal from any such action, suit or proceeding, Indemnitee shall be indemnified against all expenses (including attorneys' fees) actually and reasonably incurred by or on behalf of Indemnitee in connection therewith. Without limiting the foregoing, if any action, suit or proceeding is disposed of, on the merits or otherwise (including a disposition without prejudice), without (i) the disposition being adverse to Indemnitee, (ii) an adjudication that Indemnitee was liable to the Corporation, (iii) a plea of guilty or nolo contendere by Indemnitee, (iv) an adjudication that Indemnitee did not act in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the Corporation, and (v) with respect to any criminal proceeding, an adjudication that Indemnitee had reasonable cause to believe his or her conduct was unlawful, Indemnitee shall be considered for the purposes hereof to have been wholly successful with respect thereto.

4. Notification and Defense of Claim. As a condition precedent to an Indemnitee's right to be indemnified, such Indemnitee must notify the Corporation in writing as soon as practicable of any action, suit, proceeding or investigation involving such Indemnitee for which indemnity will or could be sought. With respect to any action, suit, proceeding or investigation of which the Corporation is so notified, the Corporation will be entitled to participate therein at

its own expense and/or to assume the defense thereof at its own expense, with legal counsel reasonably acceptable to Indemnitee. After notice from the Corporation to Indemnitee of its election so to assume such defense, the Corporation shall not be liable to Indemnitee for any legal or other expenses subsequently incurred by Indemnitee in connection with such action, suit, proceeding or investigation, other than as provided below in this Section 4. Indemnitee shall have the right to employ his or her own counsel in connection with such action, suit, proceeding or investigation, but the fees and expenses of such counsel incurred after notice from the Corporation of its assumption of the defense thereof shall be at the expense of Indemnitee unless (i) the employment of counsel by Indemnitee has been authorized by the Corporation, (ii) counsel to Indemnitee shall have reasonably concluded that there may be a conflict of interest or position on any significant issue between the Corporation and Indemnitee in the conduct of the defense of such action, suit, proceeding or investigation or (iii) the Corporation shall not in fact have employed counsel to assume the defense of such action, suit, proceeding or investigation, in each of which cases the fees and expenses of counsel for Indemnitee shall be at the expense of the Corporation, except as otherwise expressly provided by this Article EIGHTH. The Corporation shall not be entitled, without the consent of Indemnitee, to assume the defense of any claim brought by or in the right of the Corporation or as to which counsel for Indemnitee shall have reasonably made the conclusion provided for in clause (ii) above. The Corporation shall not be required to indemnify Indemnitee under this Article EIGHTH for any amounts paid in settlement of any action, suit, proceeding or investigation effected without its written consent. The Corporation shall not settle any action, suit, proceeding or investigation in any manner which would impose any penalty or limitation on Indemnitee without Indemnitee's written consent. Neither the Corporation nor Indemnitee will unreasonably withhold or delay its consent to any proposed settlement.

5. Advancement of Expenses. Subject to the provisions of Section 6 of this Article EIGHTH, in the event of any threatened or pending action, suit, proceeding or investigation of which the Corporation receives notice under this Article EIGHTH, any expenses (including attorneys' fees) incurred by or on behalf of Indemnitee in defending an action, suit, proceeding or investigation or any appeal therefrom shall be paid by the Corporation in advance of the final disposition of such matter; provided, however, that the payment of such expenses incurred by or on behalf of Indemnitee in advance of the final disposition of such matter shall be made only upon receipt of an undertaking by or on behalf of Indemnitee to repay all amounts so advanced in the event that it shall ultimately be determined by final judicial decision from which there is no further right to appeal that Indemnitee is not entitled to be indemnified by the Corporation as authorized in this Article EIGHTH; and provided further that no such advancement of expenses shall be made under this Article EIGHTH if it is determined (in the manner described in Section 6) that (i) Indemnitee did not act in good faith and in a manner he or she reasonably believed to be in, or not opposed to, the best interests of the Corporation, or (ii) with respect to any criminal action or proceeding, Indemnitee had reasonable cause to believe his or her conduct was unlawful. Such undertaking shall be accepted without reference to the financial ability of Indemnitee to make such repayment.

6. Procedure for Indemnification and Advancement of Expenses. In order to obtain indemnification or advancement of expenses pursuant to Section 1, 2, 3 or 5 of this Article EIGHTH, an Indemnitee shall submit to the Corporation a written request. Any such advancement of expenses shall be made promptly, and in any event within 60 days after receipt

by the Corporation of the written request of Indemnitee, unless (i) the Corporation has assumed the defense pursuant to Section 4 of this Article EIGHTH (and none of the circumstances described in Section 4 of this Article EIGHTH that would nonetheless entitle the Indemnitee to indemnification for the fees and expenses of separate counsel have occurred) or (ii) the Corporation determines within such 60-day period that Indemnitee did not meet the applicable standard of conduct set forth in Section 1, 2 or 5 of this Article EIGHTH, as the case may be. Any such indemnification, unless ordered by a court, shall be made with respect to requests under Section 1 or 2 of this Article EIGHTH only as authorized in the specific case upon a determination by the Corporation that the indemnification of Indemnitee is proper because Indemnitee has met the applicable standard of conduct set forth in Section 1 or 2, as the case may be. Such determination shall be made in each instance (a) by a majority vote of the directors of the Corporation consisting of persons who are not at that time parties to the action, suit or proceeding in question (“disinterested directors”), whether or not a quorum, (b) by a committee of disinterested directors designated by majority vote of disinterested directors, whether or not a quorum, (c) if there are no disinterested directors, or if the disinterested directors so direct, by independent legal counsel (who may, to the extent permitted by law, be regular legal counsel to the Corporation) in a written opinion, or (d) by the stockholders of the Corporation.

7. Remedies. Subject to Article TWELFTH, the right to indemnification or advancement of expenses as granted by this Article EIGHTH shall be enforceable by Indemnitee in any court of competent jurisdiction. Neither the failure of the Corporation to have made a determination prior to the commencement of such action that indemnification is proper in the circumstances because Indemnitee has met the applicable standard of conduct, nor an actual determination by the Corporation pursuant to Section 6 of this Article EIGHTH that Indemnitee has not met such applicable standard of conduct, shall be a defense to the action or create a presumption that Indemnitee has not met the applicable standard of conduct. In any suit brought by Indemnitee to enforce a right to indemnification or advancement of expenses, or brought by the Corporation to recover an advancement of expenses pursuant to the terms of an undertaking, the Corporation shall have the burden of proving that Indemnitee is not entitled to be indemnified, or to such advancement of expenses, under this Article EIGHTH. Indemnitee’s expenses (including attorneys’ fees) reasonably incurred in connection with successfully establishing Indemnitee’s right to indemnification or advancement of expenses, in whole or in part, in any such proceeding shall also be indemnified by the Corporation to the fullest extent permitted by applicable law. Notwithstanding the foregoing, in any suit brought by Indemnitee to enforce a right to indemnification or advancement of expenses hereunder it shall be a defense that the Indemnitee has not met any applicable standard for indemnification set forth in the General Corporation Law of the State of Delaware.

8. Limitations. Notwithstanding anything to the contrary in this Article EIGHTH, except as set forth in Section 7 of this Article EIGHTH, the Corporation shall not indemnify, or advance expenses to, an Indemnitee pursuant to this Article EIGHTH in connection with a proceeding (or part thereof) initiated by such Indemnitee unless the initiation thereof was approved by the Board of Directors. Notwithstanding anything to the contrary in this Article EIGHTH, the Corporation shall not indemnify or advance expenses to an Indemnitee to the extent such Indemnitee is reimbursed from the proceeds of insurance, and in the event the Corporation makes any indemnification or advancement payments to an Indemnitee and such Indemnitee is subsequently reimbursed from the proceeds of insurance, such Indemnitee shall

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promptly refund indemnification or advancement payments to the Corporation to the extent of such insurance reimbursement.

9. Subsequent Amendment. No amendment, termination or repeal of this Article EIGHTH or of the relevant provisions of the General Corporation Law of the State of Delaware or any other applicable laws shall adversely affect or diminish in any way the rights of any Indemnitee to indemnification or advancement of expenses under the provisions hereof with respect to any action, suit, proceeding or investigation arising out of or relating to any actions, transactions or facts occurring prior to the final adoption of such amendment, termination or repeal.

10. Other Rights. The indemnification and advancement of expenses provided by this Article EIGHTH shall not be deemed exclusive of any other rights to which an Indemnitee seeking indemnification or advancement of expenses may be entitled under any law (common or statutory), agreement or vote of stockholders or disinterested directors or otherwise, both as to action in Indemnitee’s official capacity and as to action in any other capacity while holding office for the Corporation, and shall continue as to an Indemnitee who has ceased to be a director or officer, and shall inure to the benefit of the estate, heirs, executors and administrators of Indemnitee. Nothing contained in this Article EIGHTH shall be deemed to prohibit, and the Corporation is specifically authorized to enter into, agreements with officers and directors providing indemnification and advancement rights and procedures different from those set forth in this Article EIGHTH. In addition, the Corporation may, to the extent authorized from time to time by its Board of Directors, grant indemnification and advancement rights to other employees or agents of the Corporation or other persons serving the Corporation and such rights may be equivalent to, or greater or less than, those set forth in this Article EIGHTH.

11. Partial Indemnification. If an Indemnitee is entitled under any provision of this Article EIGHTH to indemnification by the Corporation for some or a portion of the expenses (including attorneys’ fees), liabilities, losses, judgments, fines (including excise taxes and penalties arising under the Employee Retirement Income Security Act of 1974) or amounts paid in settlement actually and reasonably incurred by or on behalf of Indemnitee in connection with any action, suit, proceeding or investigation and any appeal therefrom but not, however, for the total amount thereof, the Corporation shall nevertheless indemnify Indemnitee for the portion of such expenses (including attorneys’ fees), liabilities, losses, judgments, fines (including excise taxes and penalties arising under the Employee Retirement Income Security Act of 1974) or amounts paid in settlement to which Indemnitee is entitled.

12. Insurance. The Corporation may purchase and maintain insurance, at its expense, to protect itself and any director, officer, employee or agent of the Corporation or another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan) against any expense, liability or loss incurred by him or her in any such capacity, or arising out of his or her status as such, whether or not the Corporation would have the power to indemnify such person against such expense, liability or loss under the General Corporation Law of the State of Delaware.

13. Savings Clause. If this Article EIGHTH or any portion hereof shall be invalidated on any ground by any court of competent jurisdiction, then the Corporation shall nevertheless

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indemnify each Indemnitee as to any expenses (including attorneys' fees), liabilities, losses, judgments, fines (including excise taxes and penalties arising under the Employee Retirement Income Security Act of 1974) and amounts paid in settlement in connection with any action, suit, proceeding or investigation, whether civil, criminal or administrative, including an action by or in the right of the Corporation, to the fullest extent permitted by any applicable portion of this Article EIGHTH that shall not have been invalidated and to the fullest extent permitted by applicable law.

14. Definitions. Terms used herein and defined in Section 145(h) and Section 145(i) of the General Corporation Law of the State of Delaware shall have the respective meanings assigned to such terms in such Section 145(h) and Section 145(i).

NINTH: This Article NINTH is inserted for the management of the business and for the conduct of the affairs of the Corporation.

1. General Powers. The business and affairs of the Corporation shall be managed by or under the direction of the Board of Directors.

2. Number of Directors; Election of Directors. Subject to the rights of holders of any series of Preferred Stock to elect directors, the number of directors of the Corporation shall be established from time to time by the Board of Directors. Election of directors need not be by written ballot, except as and to the extent provided in the Bylaws of the Corporation.

3. Classes of Directors. Subject to the rights of holders of any series of Preferred Stock to elect directors, the Board of Directors shall be and is divided into three classes, designated Class I, Class II and Class III. Each class shall consist, as nearly as may be possible, of one-third of the total number of directors constituting the entire Board of Directors. The Board of Directors is authorized to assign members of the Board of Directors already in office to Class I, Class II or Class III at the time such classification becomes effective.

4. Terms of Office. Subject to the rights of holders of any series of Preferred Stock to elect directors, each director shall serve for a term ending on the date of the third annual meeting of stockholders following the annual meeting of stockholders at which such director was elected; provided that each director initially assigned to Class I shall serve for a term expiring at the Corporation's first annual meeting of stockholders held after the effectiveness of this Restated Certificate of Incorporation; each director initially assigned to Class II shall serve for a term expiring at the Corporation's second annual meeting of stockholders held after the effectiveness of this Restated Certificate of Incorporation; and each director initially assigned to Class III shall serve for a term expiring at the Corporation's third annual meeting of stockholders held after the effectiveness of this Restated Certificate of Incorporation; provided further, that the term of each director shall continue until the election and qualification of his or her successor and be subject to his or her earlier death, resignation or removal.

5. Quorum. The greater of (a) a majority of the directors at any time in office and (b) one-third of the number of directors fixed pursuant to Section 2 of this Article NINTH shall constitute a quorum of the Board of Directors. If at any meeting of the Board of Directors there shall be less than such a quorum, a majority of the directors present may adjourn the meeting

from time to time without further notice other than announcement at the meeting, until a quorum shall be present.

6. Action at Meeting. Every act or decision done or made by a majority of the directors present at a meeting duly held at which a quorum is present shall be regarded as the act of the Board of Directors unless a greater number is required by law or by this Certificate of Incorporation.

7. Removal. Subject to the rights of holders of any series of Preferred Stock, directors of the Corporation may be removed only for cause and only by the affirmative vote of the holders of at least seventy-five percent (75%) of the votes that all the stockholders would be entitled to cast in an election of directors or class of directors.

8. Vacancies. Subject to the rights of holders of any series of Preferred Stock, any vacancies or newly-created directorships on the Board of Directors, however occurring, shall be filled only by vote of a majority of the directors then in office, although less than a quorum, or by a sole remaining director and shall not be filled by the stockholders. A director elected to fill a vacancy or to fill a position resulting from a newly-created directorship shall hold office until the next election of the class for which such director shall have been chosen, subject to the election and qualification of a successor and to such director's earlier death, resignation or removal.

9. Stockholder Nominations and Introduction of Business, Etc. Advance notice of stockholder nominations for election of directors and other business to be brought by stockholders before a meeting of stockholders shall be given in the manner provided by the Bylaws of the Corporation.

10. Amendments to Article. Notwithstanding any other provisions of law, this Certificate of Incorporation or the Bylaws of the Corporation, and notwithstanding the fact that a lesser percentage may be specified by law, the affirmative vote of the holders of at least seventy-five percent (75%) of the votes that all the stockholders would be entitled to cast in an election of directors or class of directors shall be required to amend or repeal, or to adopt any provision inconsistent with, this Article NINTH.

TENTH: Stockholders of the Corporation may not take any action by written consent in lieu of a meeting. Notwithstanding any other provisions of law, this Certificate of Incorporation or the Bylaws of the Corporation, and notwithstanding the fact that a lesser percentage may be specified by law, the affirmative vote of the holders of at least seventy-five percent (75%) of the votes that all the stockholders would be entitled to cast in an election of directors or class of directors shall be required to amend or repeal, or to adopt any provision inconsistent with, this Article TENTH.

ELEVENTH: Special meetings of stockholders for any purpose or purposes may be called at any time only by the Board of Directors, and may not be called by any other person or persons. Business transacted at any special meeting of stockholders shall be limited to matters relating to the purpose or purposes stated in the notice of meeting. Notwithstanding any other provisions of law, this Certificate of Incorporation or the Bylaws of the Corporation, and

notwithstanding the fact that a lesser percentage may be specified by law, the affirmative vote of the holders of at least seventy-five percent (75%) of the votes that all the stockholders would be entitled to cast in an election of directors or class of directors shall be required to amend or repeal, or to adopt any provision inconsistent with, this Article ELEVENTH.

TWELFTH: Unless the Corporation consents in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if the Court of Chancery of the State of Delaware does not have jurisdiction, the federal district court for the District of Delaware) shall, to the fullest extent permitted by law, be the sole and exclusive forum for: (i) any derivative action or proceeding brought on behalf of the Corporation, (ii) any action asserting a claim of breach of a fiduciary duty owed by any director, officer, other employee or stockholder of the Corporation to the Corporation or the Corporation's stockholders, (iii) any action asserting a claim arising pursuant to any provision of the General Corporation Law of the State of Delaware or as to which the General Corporation Law of the State of Delaware confers jurisdiction on the Court of Chancery of the State of Delaware, or (iv) any action asserting a claim arising pursuant to any provision of this Certificate of Incorporation or the Bylaws of the Corporation (in each case, as they may be amended from time to time) or governed by the internal affairs doctrine; provided that this sentence shall not apply to suits brought to enforce any duty or liability created by the Securities Act of 1933 or the rules and regulations thereunder or the Securities Exchange Act of 1934 or the rules and regulations thereunder or any claim for which the federal courts have exclusive jurisdiction.

Any person or entity purchasing or otherwise acquiring or holding any interest in shares of capital stock of the Corporation shall be deemed to have notice of and consented to the provisions of this Article TWELFTH.

IN WITNESS WHEREOF, this Restated Certificate of Incorporation, which restates, integrates and amends the certificate of incorporation of the Corporation, and which has been duly adopted in accordance with Sections 228, 242 and 245 of the General Corporation Law of the State of Delaware, has been executed by its duly authorized officer this day of , 2019.

FULCRUM THERAPEUTICS, INC.

By:

Name: Robert J. Gould

Title: President and Chief Executive Officer

AMENDED AND RESTATED BYLAWS
OF
FULCRUM THERAPEUTICS, INC.

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ARTICLE I

STOCKHOLDERS

1.1 Place of Meetings. All meetings of stockholders shall be held at such place, if any, as may be designated from time to time by the Board of Directors, the Chairman of the Board or the Chief Executive Officer or, if not so designated, at the principal executive office of the corporation. The Board of Directors may, in its sole discretion, determine that a meeting shall not be held at any place, but shall instead be held solely by means of remote communication in a manner consistent with the General Corporation Law of the State of Delaware.

1.2 Annual Meeting. The annual meeting of stockholders for the election of directors to succeed those whose terms expire and for the transaction of such other business as may properly be brought before the meeting shall be held on a date and at a time designated by the Board of Directors, the Chairman of the Board or the Chief Executive Officer. The Board of Directors may postpone, reschedule or cancel any previously scheduled annual meeting of stockholders.

1.3 Special Meetings. Special meetings of stockholders for any purpose or purposes may be called at any time only by the Board of Directors, and may not be called by any other person or persons. Business transacted at any special meeting of stockholders shall be limited to matters relating to the purpose or purposes stated in the notice of meeting. The Board of Directors may postpone, reschedule or cancel any previously scheduled special meeting of stockholders.

1.4 Record Date for Stockholder Meetings. In order that the corporation may determine the stockholders entitled to notice of any meeting of stockholders or any adjournment thereof, the Board of Directors may fix a record date, which record date shall not precede the date upon which the resolution fixing the record date is adopted by the Board of Directors, and which record date shall not be more than 60 nor less than 10 days before the date of such meeting. If the Board of Directors so fixes a date, such date shall also be the record date for determining the stockholders entitled to vote at such meeting unless the Board of Directors

determines, at the time it fixes such record date, that a later date on or before the date of the meeting shall be the date for making such determination. If no record date is fixed by the Board of Directors, the record date for determining stockholders entitled to notice of or to vote at a meeting of stockholders shall be at the close of business on the day next preceding the day on which notice is given, or, if notice is waived, at the close of business on the day next preceding the day on which the meeting is held. A determination of stockholders of record entitled to notice of or to vote at a meeting of stockholders shall apply to any adjournment of the meeting; provided, however, that the Board of Directors may fix a new record date for determination of stockholders entitled to vote at the adjourned meeting, and in such case shall also fix as the record date for stockholders entitled to notice of such adjourned meeting the same or an earlier date as that fixed for determination of stockholders entitled to vote in accordance herewith at the adjourned meeting.

1.5 Notice of Meetings. Except as otherwise provided by law, the Certificate of Incorporation or these bylaws, notice of each meeting of stockholders, whether annual or special, shall be given not less than 10 nor more than 60 days before the date of the meeting to each stockholder entitled to vote at such meeting. Without limiting the manner by which notice otherwise may be given to stockholders, any notice shall be effective if given by a form of electronic transmission consented to (in a manner consistent with the General Corporation Law of the State of Delaware) by the stockholder to whom the notice is given. The notices of all meetings shall state the place, if any, date and time of the meeting and the means of remote communications, if any, by which stockholders and proxyholders may be deemed to be present in person and vote at such meeting. The notice of a special meeting shall state, in addition, the purpose or purposes for which the meeting is called. If notice is given by mail, such notice shall be deemed given when deposited in the United States mail, postage prepaid, directed to the stockholder at such stockholder's address as it appears on the records of the corporation. If notice is given by electronic transmission, such notice shall be deemed given at the time specified in Section 232 of the General Corporation Law of the State of Delaware.

1.6 Voting List. The corporation shall prepare, at least 10 days before every meeting of stockholders, a complete list of the stockholders entitled to vote at the meeting (provided, however, if the record date for determining the stockholders entitled to vote is less than 10 days

before the meeting date, the list shall reflect the stockholders entitled to vote as of the tenth day before the meeting), arranged in alphabetical order, and showing the address of each stockholder and the number of shares registered in the name of each stockholder. Such list shall be open to the examination of any stockholder, for any purpose germane to the meeting for a period of at least 10 days prior to the meeting: (a) on a reasonably accessible electronic network, provided that the information required to gain access to such list is provided with the notice of the meeting, or (b) during ordinary business hours, at the principal place of business of the corporation. If the meeting is to be held at a physical location (and not solely by means of remote communication), then the list shall be produced and kept at the time and place of the meeting during the whole time thereof, and may be examined by any stockholder who is present. If the meeting is to be held solely by means of remote communication, then the list shall also be open to the examination of any stockholder during the whole time of the meeting on a reasonably accessible electronic network, and the information required to access such list shall be provided with the notice of the meeting. Except as otherwise provided by law, such list shall be the only evidence as to who are the stockholders entitled to examine the list of stockholders required by this Section 1.6 or to vote in person or by proxy at any meeting of stockholders.

1.7 Quorum. Except as otherwise provided by law, the Certificate of Incorporation or these bylaws, the holders of a majority in voting power of the shares of the capital stock of the corporation issued and outstanding and entitled to vote at the meeting, present in person, present by means of remote communication in a manner, if any, authorized by the Board of Directors in its sole discretion, or represented by proxy, shall constitute a quorum for the transaction of business; provided, however, that where a separate vote by a class or classes or series of capital stock is required by law or the Certificate of Incorporation, the holders of a majority in voting power of the shares of such class or classes or series of the capital stock of the corporation issued and outstanding and entitled to vote on such matter, present in person, present by means of remote communication in a manner, if any, authorized by the Board of Directors in its sole discretion, or represented by proxy, shall constitute a quorum entitled to take action with respect to the vote on such matter. A quorum, once established at a meeting, shall not be broken by the withdrawal of enough votes to leave less than a quorum.

1.8 Adjournments. Any meeting of stockholders may be adjourned from time to time to reconvene at any other time and to any other place at which a meeting of stockholders may be held under these bylaws by the chairman of the meeting. It shall not be necessary to notify any stockholder of any adjournment of less than 30 days if the time and place, if any, of the adjourned meeting, and the means of remote communication, if any, by which stockholders and proxyholders may be deemed to be present in person and vote at such adjourned meeting, are announced at the meeting at which adjournment is taken, unless after the adjournment a new record date is fixed for the adjourned meeting. At the adjourned meeting, the corporation may transact any business that might have been transacted at the original meeting. If the adjournment is for more than 30 days, a notice of the adjourned meeting shall be given to each stockholder of record entitled to vote at the meeting. If after the adjournment a new record date for determination of stockholders entitled to vote is fixed for the adjourned meeting, the Board of Directors shall fix as the record date for determining stockholders entitled to notice of such adjourned meeting the same or an earlier date as that fixed for determination of stockholders entitled to vote at the adjourned meeting, and shall give notice of the adjourned meeting to each stockholder of record as of the record date so fixed for notice of such adjourned meeting.

1.9 Voting and Proxies. Each stockholder shall have one vote upon the matter in question for each share of stock entitled to vote held of record by such stockholder and a proportionate vote for each fractional share so held, unless otherwise provided by law or the Certificate of Incorporation. Each stockholder of record entitled to vote at a meeting of stockholders may vote in person (including by means of remote communications, if any, by which stockholders may be deemed to be present in person and vote at such meeting) or may authorize another person or persons to vote for such stockholder by a proxy executed or transmitted in a manner permitted by the General Corporation Law of the State of Delaware by the stockholder or such stockholder's authorized agent and delivered (including by electronic transmission) to the Secretary of the corporation. No such proxy shall be voted upon after three years from the date of its execution, unless the proxy expressly provides for a longer period.

1.10 Action at Meeting. When a quorum is present at any meeting, any matter other than the election of directors to be voted upon by the stockholders at such meeting shall be decided by the vote of the holders of shares of stock having a majority in voting power of the

votes cast by the holders of all of the shares of stock present or represented at the meeting and voting affirmatively or negatively on such matter (or if there are two or more classes or series of stock entitled to vote as separate classes, then in the case of each such class or series, the holders of a majority in voting power of the shares of stock of that class or series present or represented at the meeting and voting affirmatively or negatively on such matter), except when a different vote is required by law, the Certificate of Incorporation or these bylaws. When a quorum is present at any meeting, any election by stockholders of directors shall be determined by a plurality of the votes cast by the stockholders entitled to vote on the election.

1.11 Nomination of Directors.

(a) Except for (1) any directors entitled to be elected by the holders of preferred stock, (2) any directors elected in accordance with Section 2.8 hereof by the Board of Directors to fill vacancies or newly-created directorships or (3) as otherwise required by applicable law or stock exchange regulation, at any meeting of stockholders, only persons who are nominated in accordance with the procedures in this Section 1.11 shall be eligible for election as directors. Nomination for election to the Board of Directors at a meeting of stockholders may be made (i) by or at the direction of the Board of Directors or (ii) by any stockholder of the corporation who (x) timely complies with the notice procedures in Section 1.11(b), (y) is a stockholder of record who is entitled to vote for the election of such nominee on the date of the giving of such notice and on the record date for the determination of stockholders entitled to vote at such meeting and (z) is entitled to vote at such meeting.

(b) To be timely, a stockholder's notice must be received in writing by the Secretary at the principal executive office of the corporation as follows: (1) in the case of an election of directors at an annual meeting of stockholders, not less than 90 days nor more than 120 days prior to the first anniversary of the preceding year's annual meeting; provided, however, that (x) in the case of an annual meeting of stockholders of the corporation to be held in 2020 or (y) in the event that the date of the annual meeting in any other year is advanced by more than 30 days, or delayed by more than 60 days, from the first anniversary of the preceding year's annual meeting, or if no annual meeting was held in the preceding year, a stockholder's notice must be so received not earlier than the 120th day prior to such annual meeting and not

later than the close of business on the later of (x) the 90th day prior to such annual meeting and (y) the tenth day following the day on which notice of the date of such annual meeting was mailed or public disclosure of the date of such annual meeting was made, whichever first occurs; or (2) in the case of an election of directors at a special meeting of stockholders, provided that the Board of Directors has determined, in accordance with Section 1.3, that directors shall be elected at such special meeting and provided further that the nomination made by the stockholder is for one of the director positions that the Board of Directors has determined will be filled at such special meeting, not earlier than the 120th day prior to such special meeting and not later than the close of business on the later of (x) the 90th day prior to such special meeting and (y) the tenth day following the day on which notice of the date of such special meeting was mailed or public disclosure of the date of such special meeting was made, whichever first occurs. In no event shall the adjournment or postponement of a meeting (or the public disclosure thereof) commence a new time period (or extend any time period) for the giving of a stockholder's notice.

The stockholder's notice to the Secretary shall set forth: (A) as to each proposed nominee (1) such person's name, age, business address and, if known, residence address, (2) such person's principal occupation or employment, (3) the class and series and number of shares of stock of the corporation that are, directly or indirectly, owned, beneficially or of record, by such person, (4) a description of all direct and indirect compensation and other material monetary agreements, arrangements and understandings during the past three years, and any other material relationships, between or among (x) the stockholder, the beneficial owner, if any, on whose behalf the nomination is being made and the respective affiliates and associates of, or others acting in concert with, such stockholder and such beneficial owner, on the one hand, and (y) each proposed nominee, and his or her respective affiliates and associates, or others acting in concert with such nominee(s), on the other hand, including all information that would be required to be disclosed pursuant to Item 404 of Regulation S-K if the stockholder making the nomination and any beneficial owner on whose behalf the nomination is made or any affiliate or associate thereof or person acting in concert therewith were the "registrant" for purposes of such Item and the proposed nominee were a director or executive officer of such registrant, and (5) any other information concerning such person that must be disclosed as to nominees in proxy solicitations pursuant to Regulation 14A under the Securities Exchange Act of 1934, as amended (the

“Exchange Act”); and (B) as to the stockholder giving the notice and the beneficial owner, if any, on whose behalf the nomination is being made (1) the name and address of such stockholder, as they appear on the corporation’s books, and of such beneficial owner, (2) the class and series and number of shares of stock of the corporation that are, directly or indirectly, owned, beneficially or of record, by such stockholder and such beneficial owner, (3) a description of any agreement, arrangement or understanding between or among such stockholder and/or such beneficial owner and each proposed nominee and any other person or persons (including their names) pursuant to which the nomination(s) are being made or who may participate in the solicitation of proxies or votes in favor of electing such nominee(s), (4) a description of any agreement, arrangement or understanding (including any derivative or short positions, swaps, profit interests, options, warrants, convertible securities, stock appreciation or similar rights, hedging transactions, and borrowed or loaned shares) that has been entered into by, or on behalf of, such stockholder or such beneficial owner, the effect or intent of which is to mitigate loss to, manage risk or benefit of share price changes for, or increase or decrease the voting power of, such stockholder or such beneficial owner with respect to shares of stock of the corporation, (5) any other information relating to such stockholder and such beneficial owner that would be required to be disclosed in a proxy statement or other filings required to be made in connection with solicitations of proxies for the election of directors in a contested election pursuant to Section 14 of the Exchange Act and the rules and regulations promulgated thereunder, (6) a representation that such stockholder intends to appear in person or by proxy at the meeting to nominate the person(s) named in its notice and (7) a representation whether such stockholder and/or such beneficial owner intends or is part of a group that intends (x) to deliver a proxy statement and/or form of proxy to holders of at least the percentage of the corporation’s outstanding capital stock reasonably believed by such stockholder or such beneficial owner to be sufficient to elect the nominee (and such representation shall be included in any such proxy statement and form of proxy) and/or (y) otherwise to solicit proxies or votes from stockholders in support of such nomination (and such representation shall be included in any such solicitation materials). Not later than 10 days after the record date for the meeting, the information required by Items (A)(1)-(5) and (B)(1)-(5) of the prior sentence shall be supplemented by the stockholder giving the notice to provide updated information as of the record date. In addition, to be effective, the stockholder’s notice must be accompanied by the written consent of the proposed

nominee to serve as a director if elected. The corporation may require any proposed nominee to furnish such other information as the corporation may reasonably require to determine the eligibility of such proposed nominee to serve as a director of the corporation or whether such nominee would be independent under applicable Securities and Exchange Commission and stock exchange rules and the corporation's publicly disclosed corporate governance guidelines. A stockholder shall not have complied with this Section 1.11(b) if the stockholder (or beneficial owner, if any, on whose behalf the nomination is made) solicits or does not solicit, as the case may be, proxies or votes in support of such stockholder's nominee in contravention of the representations with respect thereto required by this Section 1.11.

(c) The chairman of any meeting shall have the power and duty to determine whether a nomination was made in accordance with the provisions of this Section 1.11 (including whether the stockholder or beneficial owner, if any, on whose behalf the nomination is made solicited (or is part of a group that solicited) or did not so solicit, as the case may be, proxies or votes in support of such stockholder's nominee in compliance with the representations with respect thereto required by this Section 1.11), and if the chairman should determine that a nomination was not made in accordance with the provisions of this Section 1.11, the chairman shall so declare to the meeting and such nomination shall not be brought before the meeting.

(d) Except as otherwise required by law, nothing in this Section 1.11 shall obligate the corporation or the Board of Directors to include in any proxy statement or other stockholder communication distributed on behalf of the corporation or the Board of Directors information with respect to any nominee for director submitted by a stockholder.

(e) Notwithstanding the foregoing provisions of this Section 1.11, unless otherwise required by law, if the stockholder (or a qualified representative of the stockholder) does not appear at the meeting to present a nomination, such nomination shall not be brought before the meeting, notwithstanding that proxies in respect of such nominee may have been received by the corporation. For purposes of this Section 1.11, to be considered a "qualified representative of the stockholder", a person must be a duly authorized officer, manager or partner of such stockholder or must be authorized by a written instrument executed by such

stockholder or an electronic transmission delivered by such stockholder to act for such stockholder as proxy at the meeting of stockholders and such person must produce such written instrument or electronic transmission, or a reliable reproduction of the written instrument or electronic transmission, at the meeting of stockholders.

(f) For purposes of this Section 1.11, “public disclosure” shall include disclosure in a press release reported by the Dow Jones News Service, Associated Press or comparable national news service or in a document publicly filed by the corporation with the Securities and Exchange Commission pursuant to Section 13, 14 or 15(d) of the Exchange Act.

1.12 Notice of Business at Annual Meetings.

(a) At any annual meeting of the stockholders, only such business shall be conducted as shall have been properly brought before the meeting. To be properly brought before an annual meeting, business must be (1) specified in the notice of meeting (or any supplement thereto) given by or at the direction of the Board of Directors, (2) otherwise properly brought before the meeting by or at the direction of the Board of Directors, or (3) properly brought before the meeting by a stockholder. For business to be properly brought before an annual meeting by a stockholder, (i) if such business relates to the nomination of a person for election as a director of the corporation, the procedures in Section 1.11 must be complied with and (ii) if such business relates to any other matter, the business must constitute a proper matter under Delaware law for stockholder action and the stockholder must (x) have given timely notice thereof in writing to the Secretary in accordance with the procedures in Section 1.12(b), (y) be a stockholder of record who is entitled to vote on such business on the date of the giving of such notice and on the record date for the determination of stockholders entitled to vote at such annual meeting and (z) be entitled to vote at such annual meeting.

(b) To be timely, a stockholder’s notice must be received in writing by the Secretary at the principal executive office of the corporation not less than 90 days nor more than 120 days prior to the first anniversary of the preceding year’s annual meeting; provided, however, that in the event that the date of the annual meeting is advanced by more than 30 days, or delayed by more than 60 days, from the first anniversary of the preceding year’s annual meeting, or if no annual meeting was held in the preceding year, a stockholder’s notice must be

so received not earlier than the 120th day prior to such annual meeting and not later than the close of business on the later of (x) the 90th day prior to such annual meeting and (y) the tenth day following the day on which notice of the date of such annual meeting was mailed or public disclosure of the date of such annual meeting was made, whichever first occurs. In no event shall the adjournment or postponement of an annual meeting (or the public disclosure thereof) commence a new time period (or extend any time period) for the giving of a stockholder's notice.

The stockholder's notice to the Secretary shall set forth: (A) as to each matter the stockholder proposes to bring before the annual meeting (1) a brief description of the business desired to be brought before the annual meeting, (2) the text of the proposal (including the exact text of any resolutions proposed for consideration and, in the event that such business includes a proposal to amend the bylaws, the exact text of the proposed amendment), and (3) the reasons for conducting such business at the annual meeting, and (B) as to the stockholder giving the notice and the beneficial owner, if any, on whose behalf the proposal is being made (1) the name and address of such stockholder, as they appear on the corporation's books, and of such beneficial owner, (2) the class and series and number of shares of stock of the corporation that are, directly or indirectly, owned, beneficially or of record, by such stockholder and such beneficial owner, (3) a description of any material interest of such stockholder or such beneficial owner and the respective affiliates and associates of, or others acting in concert with, such stockholder or such beneficial owner in such business, (4) a description of any agreement, arrangement or understanding between or among such stockholder and/or such beneficial owner and any other person or persons (including their names) in connection with the proposal of such business or who may participate in the solicitation of proxies in favor of such proposal, (5) a description of any agreement, arrangement or understanding (including any derivative or short positions, swaps, profit interests, options, warrants, convertible securities, stock appreciation or similar rights, hedging transactions, and borrowed or loaned shares) that has been entered into by, or on behalf of, such stockholder or such beneficial owner, the effect or intent of which is to mitigate loss to, manage risk or benefit of share price changes for, or increase or decrease the voting power of, such stockholder or such beneficial owner with respect to shares of stock of the corporation, (6) any other information relating to such stockholder and such beneficial owner that would be required to be disclosed in a proxy statement or other filings required to be made

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in connection with solicitations of proxies for the business proposed pursuant to Section 14 of the Exchange Act and the rules and regulations promulgated thereunder, (7) a representation that such stockholder intends to appear in person or by proxy at the annual meeting to bring such business before the meeting and (8) a representation whether such stockholder and/or such beneficial owner intends or is part of a group that intends (x) to deliver a proxy statement and/or form of proxy to holders of at least the percentage of the corporation's outstanding capital stock required to approve or adopt the proposal (and such representation shall be included in any such proxy statement and form of proxy) and/or (y) otherwise to solicit proxies or votes from stockholders in support of such proposal (and such representation shall be included in any such solicitation materials). Not later than 10 days after the record date for the meeting, the information required by Items (A)(3) and (B)(1)-(6) of the prior sentence shall be supplemented by the stockholder giving the notice to provide updated information as of the record date. Notwithstanding anything in these bylaws to the contrary, no business shall be conducted at any annual meeting of stockholders except in accordance with the procedures in this Section 1.12; provided that any stockholder proposal that complies with Rule 14a-8 of the proxy rules (or any successor provision) promulgated under the Exchange Act and is to be included in the corporation's proxy statement for an annual meeting of stockholders shall be deemed to comply with the notice requirements of this Section 1.12. A stockholder shall not have complied with this Section 1.12(b) if the stockholder (or beneficial owner, if any, on whose behalf the proposal is made) solicits or does not solicit, as the case may be, proxies or votes in support of such stockholder's proposal in contravention of the representations with respect thereto required by this Section 1.12.

(c) The chairman of any annual meeting shall have the power and duty to determine whether business was properly brought before the annual meeting in accordance with the provisions of this Section 1.12 (including whether the stockholder or beneficial owner, if any, on whose behalf the proposal is made solicited (or is part of a group that solicited) or did not so solicit, as the case may be, proxies or votes in support of such stockholder's proposal in compliance with the representation with respect thereto required by this Section 1.12), and if the chairman should determine that business was not properly brought before the annual meeting in accordance with the provisions of this Section 1.12, the chairman shall so declare to the meeting and such business shall not be brought before the annual meeting.

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(d) Except as otherwise required by law, nothing in this Section 1.12 shall obligate the corporation or the Board of Directors to include in any proxy statement or other stockholder communication distributed on behalf of the corporation or the Board of Directors information with respect to any proposal submitted by a stockholder.

(e) Notwithstanding the foregoing provisions of this Section 1.12, unless otherwise required by law, if the stockholder (or a qualified representative of the stockholder) does not appear at the annual meeting to present business, such business shall not be considered, notwithstanding that proxies in respect of such business may have been received by the corporation.

(f) For purposes of this Section 1.12, the terms “qualified representative of the stockholder” and “public disclosure” shall have the same meaning as in Section 1.11.

1.13 Conduct of Meetings.

(a) Unless otherwise provided by the Board of Directors, meetings of stockholders shall be presided over by the Chairman of the Board, if any, or in the Chairman’s absence by the Vice Chairman of the Board, if any, or in the Vice Chairman’s absence by the Chief Executive Officer, or in the Chief Executive Officer’s absence by the President, or in the President’s absence by a Vice President, or in the absence of all of the foregoing persons by a chairman designated by the Board of Directors. The Secretary shall act as secretary of the meeting, but in the Secretary’s absence the chairman of the meeting may appoint any person to act as secretary of the meeting.

(b) The Board of Directors may adopt by resolution such rules, regulations and procedures for the conduct of any meeting of stockholders of the corporation as it shall deem appropriate including, without limitation, such guidelines and procedures as it may deem appropriate regarding the participation by means of remote communication of stockholders and proxyholders not physically present at a meeting. Except to the extent inconsistent with such rules, regulations and procedures as adopted by the Board of Directors, the chairman of any meeting of stockholders shall have the right and authority to convene and (for any or no reason) to recess and/or adjourn the meeting and prescribe such rules, regulations and procedures and to

do all such acts as, in the judgment of such chairman, are appropriate for the proper conduct of the meeting. Such rules, regulations or procedures, whether adopted by the Board of Directors or prescribed by the chairman of the meeting, may include, without limitation, the following: (i) the establishment of an agenda or order of business for the meeting; (ii) rules and procedures for maintaining order at the meeting and the safety of those present; (iii) limitations on attendance at or participation in the meeting to stockholders entitled to vote at the meeting, their duly authorized and constituted proxies or such other persons as shall be determined; (iv) restrictions on entry to the meeting after the time fixed for the commencement thereof; and (v) limitations on the time allotted to questions or comments by participants. Unless and to the extent determined by the Board of Directors or the chairman of the meeting, meetings of stockholders shall not be required to be held in accordance with the rules of parliamentary procedure.

(c) The chairman of the meeting shall announce at the meeting when the polls for each matter to be voted upon at the meeting will be opened and closed. After the polls close, no ballots, proxies or votes or any revocations or changes thereto may be accepted.

(d) In advance of any meeting of stockholders, the Board of Directors, the Chairman of the Board, the Chief Executive Officer or the President shall appoint one or more inspectors of election to act at the meeting and make a written report thereof. One or more other persons may be designated as alternate inspectors to replace any inspector who fails to act. If no inspector or alternate is present, ready and willing to act at a meeting of stockholders, the chairman of the meeting shall appoint one or more inspectors to act at the meeting. Unless otherwise required by law, inspectors may be officers, employees or agents of the corporation. Each inspector, before entering upon the discharge of such inspector's duties, shall take and sign an oath faithfully to execute the duties of inspector with strict impartiality and according to the best of such inspector's ability. The inspector shall have the duties prescribed by law and shall take charge of the polls and, when the vote is completed, shall make a certificate of the result of the vote taken and of such other facts as may be required by law. Every vote taken by ballots shall be counted by a duly appointed inspector or duly appointed inspectors.

1.14 No Action by Consent in Lieu of a Meeting. Stockholders of the corporation may not take any action by written consent in lieu of a meeting.

ARTICLE II

DIRECTORS

2.1 General Powers. The business and affairs of the corporation shall be managed by or under the direction of a Board of Directors, who may exercise all of the powers of the corporation except as otherwise provided by law or the Certificate of Incorporation.

2.2 Number, Election and Qualification. The number of directors of the corporation shall be the number fixed by, or determined in the manner provided in, the Certificate of Incorporation. Election of directors need not be by written ballot. Directors need not be stockholders of the corporation.

2.3 Chairman of the Board; Vice Chairman of the Board. The Board of Directors may appoint from its members a Chairman of the Board and a Vice Chairman of the Board, neither of whom need be an employee or officer of the corporation. If the Board of Directors appoints a Chairman of the Board, such Chairman shall perform such duties and possess such powers as are assigned by the Board of Directors and, if the Chairman of the Board is also designated as the corporation's Chief Executive Officer, shall have the powers and duties of the Chief Executive Officer prescribed in Section 3.7 of these bylaws. If the Board of Directors appoints a Vice Chairman of the Board, such Vice Chairman shall perform such duties and possess such powers as are assigned by the Board of Directors or the Chairman of the Board. Unless otherwise provided by the Board of Directors, the Chairman of the Board or, in the Chairman's absence, the Vice Chairman of the Board, if any, shall preside at all meetings of the Board of Directors.

2.4 Terms of Office. Directors shall be elected for such terms and in the manner provided by the Certificate of Incorporation and applicable law. The term of each director shall continue until the election and qualification of his or her successor and be subject to his or her earlier death, resignation or removal.

2.5 Quorum. The greater of (a) a majority of the directors at any time in office and (b) one-third of the number of directors established by the Board of Directors pursuant to the Certificate of Incorporation shall constitute a quorum of the Board of Directors. If at any meeting of the Board of Directors there shall be less than such a quorum, a majority of the directors present may adjourn the meeting from time to time without further notice other than announcement at the meeting, until a quorum shall be present.

2.6 Action at Meeting. Every act or decision done or made by a majority of the directors present at a meeting duly held at which a quorum is present shall be regarded as the act of the Board of Directors, unless a greater number is required by law or by the Certificate of Incorporation.

2.7 Removal. Directors of the corporation may be removed in the manner specified by the Certificate of Incorporation and applicable law.

2.8 Vacancies. Any vacancy or newly-created directorship on the Board of Directors, however occurring, shall be filled in the manner specified by the Certificate of Incorporation and applicable law.

2.9 Resignation. Any director may resign by delivering a resignation in writing or by electronic transmission to the corporation at its principal executive office or to the Chairman of the Board, the Chief Executive Officer, the President or the Secretary. Such resignation shall be effective upon receipt unless it is specified to be effective at some later time or upon the happening of some later event.

2.10 Regular Meetings. Regular meetings of the Board of Directors may be held without notice at such time and place as shall be determined from time to time by the Board of Directors; provided that any director who is absent when such a determination is made shall be given notice of the determination. A regular meeting of the Board of Directors may be held without notice immediately after and at the same place as the annual meeting of stockholders.

2.11 Special Meetings. Special meetings of the Board of Directors may be held at any time and place designated in a call by the Chairman of the Board, the Chief Executive Officer,

the President, two or more directors, or by one director in the event that there is only a single director in office.

2.12 Notice of Special Meetings. Notice of the date, place and time of any special meeting of directors shall be given to each director by the Secretary or by the officer or one of the directors calling the meeting. Notice shall be duly given to each director (a) in person, by telephone or by electronic transmission at least 24 hours in advance of the meeting, (b) by delivering written notice by hand to such director's last known business or home address at least 48 hours in advance of the meeting, or (c) by sending written notice by first-class mail to such director's last known business or home address at least 72 hours in advance of the meeting. A notice or waiver of notice of a meeting of the Board of Directors need not specify the purposes of the meeting.

2.13 Meetings by Conference Communications Equipment. Directors may participate in meetings of the Board of Directors or any committee thereof by means of conference telephone or other communications equipment by means of which all persons participating in the meeting can hear each other, and participation by such means shall constitute presence in person at such meeting.

2.14 Action by Consent. Any action required or permitted to be taken at any meeting of the Board of Directors or of any committee thereof may be taken without a meeting, if all members of the Board of Directors or committee, as the case may be, consent to the action in writing or by electronic transmission, and the written consents or electronic transmissions are filed with the minutes of proceedings of the Board of Directors or committee. Such filing shall be in paper form if the minutes are maintained in paper form and shall be in electronic form if the minutes are maintained in electronic form.

2.15 Committees. The Board of Directors may designate one or more committees, each committee to consist of one or more of the directors of the corporation with such lawfully delegable powers and duties as the Board of Directors thereby confers, to serve at the pleasure of the Board of Directors. The Board of Directors may designate one or more directors as alternate members of any committee, who may replace any absent or disqualified member at any meeting of the committee. In the absence or disqualification of a member of a committee, the member or

members of the committee present at any meeting and not disqualified from voting, whether or not such member or members constitute a quorum, may unanimously appoint another member of the Board of Directors to act at the meeting in the place of any such absent or disqualified member. Any such committee, to the extent provided in the resolution of the Board of Directors and subject to the provisions of law, shall have and may exercise all the powers and authority of the Board of Directors in the management of the business and affairs of the corporation and may authorize the seal of the corporation to be affixed to all papers that may require it. Each such committee shall keep minutes and make such reports as the Board of Directors may from time to time request. Except as the Board of Directors may otherwise determine, any committee may make rules for the conduct of its business, but unless otherwise provided by the directors or in such rules, its business shall be conducted as nearly as possible in the same manner as is provided in these bylaws for the Board of Directors. Except as otherwise provided in the Certificate of Incorporation, these bylaws, or the resolution of the Board of Directors designating the committee, a committee may create one or more subcommittees, each subcommittee to consist of one or more members of the committee, and delegate to a subcommittee any or all of the powers and authority of the committee.

2.16 Compensation of Directors. Directors may be paid such compensation for their services and such reimbursement for expenses of attendance at meetings as the Board of Directors may from time to time determine. No such payment shall preclude any director from serving the corporation or any of its parent or subsidiary entities in any other capacity and receiving compensation for such service.

ARTICLE III

OFFICERS

3.1 Titles. The officers of the corporation shall consist of a Chief Executive Officer, a President, a Secretary, a Treasurer and such other officers with such other titles as the Board of Directors shall determine, including one or more Vice Presidents, Assistant Treasurers and Assistant Secretaries. The Board of Directors may appoint such other officers as it may deem appropriate.

3.2 Election. The Chief Executive Officer, President, Treasurer and Secretary shall be elected annually by the Board of Directors at its first meeting following the annual meeting of stockholders. Other officers may be appointed by the Board of Directors at such meeting or at any other meeting.

3.3 Qualification. No officer need be a stockholder. Any two or more offices may be held by the same person.

3.4 Tenure. Except as otherwise provided by law, by the Certificate of Incorporation or by these bylaws, each officer shall hold office until such officer's successor is elected and qualified, unless a different term is specified in the resolution electing or appointing such officer, or until such officer's earlier death, resignation or removal.

3.5 Resignation and Removal. Any officer may resign by delivering a resignation in writing or by electronic transmission to the corporation at its principal executive office or to the Chief Executive Officer, the President or the Secretary. Such resignation shall be effective upon receipt unless it is specified to be effective at some later time or upon the happening of some later event. Any officer may be removed at any time, with or without cause, by vote of a majority of the directors then in office. Except as the Board of Directors may otherwise determine, no officer who resigns or is removed shall have any right to any compensation as an officer for any period following such officer's resignation or removal, or any right to damages on account of such removal, whether such officer's compensation be by the month or by the year or otherwise, unless such compensation is expressly provided for in a duly authorized written agreement with the corporation.

3.6 Vacancies. The Board of Directors may fill any vacancy occurring in any office for any reason and may, in its discretion, leave unfilled for such period as it may determine any offices. Each such successor shall hold office for the unexpired term of such officer's predecessor and until a successor is elected and qualified, or until such officer's earlier death, resignation or removal.

3.7 President; Chief Executive Officer. Unless the Board of Directors has designated another person as the corporation's Chief Executive Officer, the President shall be the Chief

Executive Officer of the corporation. The Chief Executive Officer shall have general charge and supervision of the business of the corporation subject to the direction of the Board of Directors, and shall perform all duties and have all powers that are commonly incident to the office of the chief executive or that are delegated to such officer by the Board of Directors. The President shall perform such other duties and shall have such other powers as the Board of Directors or the Chief Executive Officer (if the President is not the Chief Executive Officer) may from time to time prescribe. In the event of the absence, inability or refusal to act of the Chief Executive Officer or the President (if the President is not the Chief Executive Officer), the Vice President (or if there shall be more than one, the Vice Presidents in the order determined by the Board of Directors) shall perform the duties of the Chief Executive Officer and when so performing such duties shall have all the powers of and be subject to all the restrictions upon the Chief Executive Officer.

3.8 Vice Presidents. Each Vice President shall perform such duties and possess such powers as the Board of Directors or the Chief Executive Officer may from time to time prescribe. The Board of Directors may assign to any Vice President the title of Executive Vice President, Senior Vice President or any other title selected by the Board of Directors.

3.9 Secretary and Assistant Secretaries. The Secretary shall perform such duties and shall have such powers as the Board of Directors or the Chief Executive Officer may from time to time prescribe. In addition, the Secretary shall perform such duties and have such powers as are incident to the office of the secretary, including without limitation the duty and power to give notices of all meetings of stockholders and special meetings of the Board of Directors, to attend all meetings of stockholders and the Board of Directors and keep a record of the proceedings, to maintain a stock ledger and prepare lists of stockholders and their addresses as required, to be custodian of corporate records and the corporate seal and to affix and attest to the same on documents.

Any Assistant Secretary shall perform such duties and possess such powers as the Board of Directors, the Chief Executive Officer or the Secretary may from time to time prescribe. In the event of the absence, inability or refusal to act of the Secretary, the Assistant Secretary (or if

there shall be more than one, the Assistant Secretaries in the order determined by the Board of Directors) shall perform the duties and exercise the powers of the Secretary.

In the absence of the Secretary or any Assistant Secretary at any meeting of stockholders or directors, the chairman of the meeting shall designate a temporary secretary to keep a record of the meeting.

3.10 Treasurer and Assistant Treasurers. The Treasurer shall perform such duties and shall have such powers as may from time to time be assigned by the Board of Directors or the Chief Executive Officer. In addition, the Treasurer shall perform such duties and have such powers as are incident to the office of treasurer, including without limitation the duty and power to keep and be responsible for all funds and securities of the corporation, to deposit funds of the corporation in depositories selected in accordance with these bylaws, to disburse such funds as ordered by the Board of Directors, to make proper accounts of such funds, and to render as required by the Board of Directors statements of all such transactions and of the financial condition of the corporation.

The Assistant Treasurers shall perform such duties and possess such powers as the Board of Directors, the Chief Executive Officer or the Treasurer may from time to time prescribe. In the event of the absence, inability or refusal to act of the Treasurer, the Assistant Treasurer (or if there shall be more than one, the Assistant Treasurers in the order determined by the Board of Directors) shall perform the duties and exercise the powers of the Treasurer.

3.11 Salaries. Officers of the corporation shall be entitled to such salaries, compensation or reimbursement as shall be fixed or allowed from time to time by the Board of Directors.

3.12 Delegation of Authority. The Board of Directors may from time to time delegate the powers or duties of any officer to any other officer or agent, notwithstanding any provision hereof.

ARTICLE IV

CAPITAL STOCK

4.1 Issuance of Stock. Subject to the provisions of the Certificate of Incorporation, the whole or any part of any unissued balance of the authorized capital stock of the corporation or the whole or any part of any shares of the authorized capital stock of the corporation held in the corporation's treasury may be issued, sold, transferred or otherwise disposed of by vote of the Board of Directors in such manner, for such lawful consideration and on such terms as the Board of Directors may determine.

4.2 Stock Certificates; Uncertificated Shares. The shares of the corporation shall be represented by certificates, provided that the Board of Directors may provide by resolution or resolutions that some or all of any or all classes or series of the corporation's stock shall be uncertificated shares. Any such resolution shall not apply to shares represented by a certificate until such certificate is surrendered to the corporation. Every holder of stock of the corporation represented by certificates shall be entitled to have a certificate, in such form as may be prescribed by law and by the Board of Directors, representing the number of shares held by such holder registered in certificate form. Each such certificate shall be signed in a manner that complies with Section 158 of the General Corporation Law of the State of Delaware.

Each certificate for shares of stock that are subject to any restriction on transfer pursuant to the Certificate of Incorporation, these bylaws, applicable securities laws or any agreement among any number of stockholders or among such holders and the corporation shall have conspicuously noted on the face or back of the certificate either the full text of the restriction or a statement of the existence of such restriction.

If the corporation shall be authorized to issue more than one class of stock or more than one series of any class, the powers, designations, preferences and relative, participating, optional or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights shall be set forth in full or summarized on the face or back of each certificate representing shares of such class or series of stock, provided that in lieu of the foregoing requirements there may be set forth on the face or back of each certificate

representing shares of such class or series of stock a statement that the corporation will furnish without charge to each stockholder who so requests a copy of the full text of the powers, designations, preferences and relative, participating, optional or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights.

Within a reasonable time after the issuance or transfer of uncertificated shares, the registered owner thereof shall be given a notice, in writing or by electronic transmission, containing the information required to be set forth or stated on certificates pursuant to Sections 151, 156, 202(a) or 218(a) of the General Corporation Law of the State of Delaware or, with respect to Section 151 of the General Corporation Law of the State of Delaware, a statement that the corporation will furnish without charge to each stockholder who so requests the powers, designations, preferences and relative participating, optional or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights.

4.3 Transfers. Shares of stock of the corporation shall be transferable in the manner prescribed by law and in these bylaws. Transfers of shares of stock of the corporation shall be made only on the books of the corporation or by transfer agents designated to transfer shares of stock of the corporation. Subject to applicable law, shares of stock represented by certificates shall be transferred only on the books of the corporation by the surrender to the corporation or its transfer agent of the certificate representing such shares properly endorsed or accompanied by a written assignment or power of attorney properly executed, and with such proof of authority or the authenticity of signature as the corporation or its transfer agent may reasonably require. Uncertificated shares may be transferred by delivery of a written assignment or power of attorney properly executed, and with such proof of authority or the authenticity of signature as the corporation or its transfer agent may reasonably require. Except as may be otherwise required by law, by the Certificate of Incorporation or by these bylaws, the corporation shall be entitled to treat the record holder of stock as shown on its books as the owner of such stock for all purposes, including the payment of dividends and the right to vote with respect to such stock, regardless of any transfer, pledge or other disposition of such stock until the shares have been transferred on the books of the corporation in accordance with the requirements of these bylaws.

4.4 Lost, Stolen or Destroyed Certificates. The corporation may issue a new certificate of stock in place of any previously issued certificate alleged to have been lost, stolen or destroyed, upon such terms and conditions as the corporation may prescribe, including the presentation of reasonable evidence of such loss, theft or destruction and the giving of such indemnity and posting of such bond as the corporation may require for the protection of the corporation or any transfer agent or registrar.

4.5 Regulations. The issue, transfer, conversion and registration of shares of stock of the corporation shall be governed by such other regulations as the Board of Directors may establish.

ARTICLE V

GENERAL PROVISIONS

5.1 Fiscal Year. Except as from time to time otherwise designated by the Board of Directors, the fiscal year of the corporation shall begin on the first day of January of each year and end on the last day of December in each year.

5.2 Corporate Seal. The corporate seal shall be in such form as shall be approved by the Board of Directors.

5.3 Record Date for Purposes Other Than Stockholder Meetings. In order that the corporation may determine the stockholders entitled to receive payment of any dividend or other distribution or allotment of any rights, entitled to exercise any rights in respect of any change, conversion or exchange of stock, or for the purpose of any other lawful action (other than with respect to determining stockholders entitled to notice of or to vote at a meeting of stockholders, which is addressed in Section 1.4 of these bylaws), the Board of Directors may fix a record date, which shall not precede the date upon which the resolution fixing the record date is adopted, and which record date shall not be more than 60 days prior to such action. If no such record date is fixed, the record date for determining stockholders for any such purpose shall be at the close of business on the day on which the Board of Directors adopts the resolution relating thereto.

5.4 Waiver of Notice. Whenever notice is required to be given by law, by the Certificate of Incorporation or by these bylaws, a written waiver signed by the person entitled to notice, or a waiver by electronic transmission by the person entitled to notice, whether provided before, at or after the time of the event for which notice is to be given, shall be deemed equivalent to notice required to be given to such person. Neither the business nor the purpose of any meeting need be specified in any such waiver. Attendance of a person at a meeting shall constitute a waiver of notice of such meeting, except when the person attends a meeting for the express purpose of objecting at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened.

5.5 Voting of Securities. Except as the Board of Directors may otherwise designate, the Chief Executive Officer, the President or the Treasurer may waive notice of, vote, or appoint any person or persons to vote, on behalf of the corporation at, and act as, or appoint any person or persons to act as, proxy or attorney-in-fact for this corporation (with or without power of substitution) at, any meeting of stockholders or securityholders of any other entity, the securities of which may be held by this corporation, or with respect to the execution of any written or electronic consent in the name of the corporation as a holder of such securities.

5.6 Evidence of Authority. A certificate by the Secretary, or an Assistant Secretary, or a temporary Secretary, as to any action taken by the stockholders, directors, a committee or any officer or representative of the corporation shall as to all persons who rely on the certificate in good faith be conclusive evidence of such action.

5.7 Certificate of Incorporation. All references in these bylaws to the Certificate of Incorporation shall be deemed to refer to the Certificate of Incorporation of the corporation, as amended and/or restated and in effect from time to time.

5.8 Severability. Any determination that any provision of these bylaws is for any reason inapplicable, illegal or ineffective shall not affect or invalidate any other provision of these bylaws.

5.9 Pronouns. All pronouns used in these bylaws shall be deemed to refer to the masculine, feminine or neuter, singular or plural, as the identity of the person or persons may require.

ARTICLE VI

AMENDMENTS

These bylaws may be altered, amended or repealed, in whole or in part, or new bylaws may be adopted by the Board of Directors or by the stockholders as provided in the Certificate of Incorporation.

ZQ|CERT#|COY|CLS|RGSTRY|ACCT#|TRANSTYPER|RUN#|TRANS#

PO BOX 41044, Providence, RI 02946-8104
 WELLS FARGO
 CUSIP NUMBER (F/NV)
 A001
 A002
 A003
 A004

CUSIP IDENTIFIER XXXXXX XX X
 Holder ID XXXXXXXXXX
 Insurance Value 1,000,000.00
 Number of Shares 123456
 DTC 12345678 123456789012345
 Certificate Numbers
 NumNo. Denom. Total
 1 1 1
 2 2 2
 3 3 3
 4 4 4
 5 5 5
 6 6 6
 7 7 7
 Total Transaction

COMMON STOCK
PAR VALUE \$0.001

Certificate Number
ZQ00000000



FULCRUM THERAPEUTICS, INC.
INCORPORATED UNDER THE LAWS OF THE STATE OF DELAWARE

THIS CERTIFIES THAT

MR. SAMPLE & MRS. SAMPLE & MR. SAMPLE & MRS. SAMPLE

is the owner of

ZERO HUNDRED THOUSAND ZERO HUNDRED AND ZERO

FULLY-PAID AND NON-ASSESSABLE SHARES OF COMMON STOCK OF

Fulcrum Therapeutics, Inc. (hereinafter called the "Company"), transferable on the books of the Company in person or by duly authorized attorney, upon surrender of this Certificate properly endorsed. This Certificate and the shares represented hereby, are issued and shall be held subject to all of the provisions of the Certificate of Incorporation, as amended, and the By-Laws, as amended, of the Company (copies of which are on file with the Company and with the Transfer Agent), to all of which each holder, by acceptance hereof, assents. This Certificate is not valid unless countersigned and registered by the Transfer Agent and Registrar.

Witness the facsimile seal of the Company and the facsimile signatures of its duly authorized officers.

DATED **00-00-0000**
 COUNTERSIGNED AND REGISTERED:
COMPUTERSHARE TRUST COMPANY, N.A.
 TRANSFER AGENT AND REGISTRAR.

Chief Executive Officer _____
 Chief Operating Officer _____

By _____ AUTHORIZED SIGNATURE

COMMON STOCK

Shares
*****000000*****
*****000000*****
*****000000*****
*****000000*****

SEE REVERSE FOR CERTAIN DEFINITIONS
 CUSIP **359616 10 9**

THIS CERTIFICATE IS TRANSFERABLE IN CITIES DESIGNATED BY THE TRANSFER AGENT, AVAILABLE ONLINE AT www.computershare.com

1234567

FULCRUM THERAPEUTICS, INC.

THE COMPANY WILL FURNISH WITHOUT CHARGE TO EACH SHAREHOLDER WHO SO REQUESTS, A SUMMARY OF THE POWERS, DESIGNATIONS, PREFERENCES AND RELATIVE, PARTICIPATING, OPTIONAL OR OTHER SPECIAL RIGHTS OF EACH CLASS OF STOCK OF THE COMPANY AND THE QUALIFICATIONS, LIMITATIONS OR RESTRICTIONS OF SUCH PREFERENCES AND RIGHTS, AND THE VARIATIONS IN RIGHTS, PREFERENCES AND LIMITATIONS DETERMINED FOR EACH SERIES, WHICH ARE FIXED BY THE CERTIFICATE OF INCORPORATION OF THE COMPANY, AS AMENDED, AND THE RESOLUTIONS OF THE BOARD OF DIRECTORS OF THE COMPANY, AND THE AUTHORITY OF THE BOARD OF DIRECTORS TO DETERMINE VARIATIONS FOR FUTURE SERIES. SUCH REQUEST MAY BE MADE TO THE OFFICE OF THE SECRETARY OF THE COMPANY OR TO THE TRANSFER AGENT. THE BOARD OF DIRECTORS MAY REQUIRE THE OWNER OF A LOST OR DESTROYED STOCK CERTIFICATE, OR HIS LEGAL REPRESENTATIVES, TO GIVE THE COMPANY A BOND TO INDEMNIFY IT AND ITS TRANSFER AGENTS AND REGISTRARS AGAINST ANY CLAIM THAT MAY BE MADE AGAINST THEM ON ACCOUNT OF THE ALLEGED LOSS OR DESTRUCTION OF ANY SUCH CERTIFICATE.

The following abbreviations, when used in the inscription on the face of this certificate, shall be construed as though they were written out in full according to applicable laws or regulations:

TEN COM - as tenants in common	UNIF GIFT MIN ACT Custodian.....
		(Cust) (Minor)
TEN ENT - as tenants by the entireties		under Uniform Gifts to Minors Act.....
		(State)
JT TEN - as joint tenants with right of survivorship and not as tenants in common	UNIF TRF MINACT Custodian (until age.....)
		(Cust) (Minor) under Uniform Transfers to Minors Act.....
		(State)

Additional abbreviations may also be used though not in the above list.

PLEASE INSERT SOCIAL SECURITY OR OTHER IDENTIFYING NUMBER OF ASSIGNEE

For value received, _____ hereby sell, assign and transfer unto

of the Common Stock represented by the within Certificate, and do hereby irrevocably constitute and appoint _____ Shares
to transfer the said stock on the books of the within-named Company with full power of substitution in the premises. _____ Attorney

Dated: _____ 20 _____

Signature: _____

Signature: _____

Notice: The signature to this assignment must correspond with the name as written upon the face of the certificate, in every particular, without alteration or enlargement, or any change whatever.

Signature(s) Guaranteed: Medallion Guarantee Stamp
THE SIGNATURE(S) SHOULD BE GUARANTEED BY AN ELIGIBLE GUARANTOR INSTITUTION (Banks, Stockbrokers, Savings and Loan Associations and Credit Unions) WITH MEMBERSHIP IN AN APPROVED SIGNATURE GUARANTEE MEDALLION PROGRAM, PURSUANT TO S.E.C. RULE 17Ad-15.

SECURITY INSTRUCTIONS

THIS IS WATERMARKED PAPER. DO NOT ACCEPT WITHOUT NOTING WATERMARK. HOLD TO LIGHT TO VERIFY WATERMARK.



The IRS requires that the named transfer agent ("we") report the cost basis of certain shares or units acquired after January 1, 2011. If your shares or units are covered by the legislation, and you requested to sell or transfer the shares or units using a specific cost basis calculation method, then we have processed as you requested. If you did not specify a cost basis calculation method, then we have defaulted to the first in, first out (FIFO) method. Please consult your tax advisor if you need additional information about cost basis.

If you do not keep in contact with the issuer or do not have any activity in your account for the time period specified by state law, your property may become subject to state unclaimed property laws and transferred to the appropriate state.

1534201

FULCRUM THERAPEUTICS, INC.
AMENDED AND RESTATED INVESTORS' RIGHTS AGREEMENT
August 24, 2018

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FULCRUM THERAPEUTICS, INC.

AMENDED AND RESTATED INVESTORS' RIGHTS AGREEMENT

THIS AMENDED AND RESTATED INVESTORS' RIGHTS AGREEMENT (this "**Agreement**") is made as of August 24, 2018, by and among Fulcrum Therapeutics, Inc., a Delaware corporation (the "**Company**"), and each investor listed on Schedule A hereto, each of which is referred to in this Agreement as an "**Investor**."

RECITALS:

WHEREAS, certain of the Investors (the "**Existing Investors**") hold shares of the Company's Series A Preferred Stock and/or shares of Common Stock issued upon conversion thereof and possess registration rights, information rights, rights of first offer, and other rights pursuant to that certain Investors' Rights Agreement, dated as of July 18, 2016, by and among the Company and such Existing Investors (the "**Prior Agreement**");

WHEREAS, pursuant to Section 6.6 of the Prior Agreement, the Prior Agreement may be amended by written consent of the Company and the holders of at least a majority in interest of the Registrable Securities of the Company (as defined in the Prior Agreement);

WHEREAS, certain of the Investors are parties to that certain Series B Preferred Stock Purchase Agreement of even date herewith by and among the Company and such Investors (the "**Purchase Agreement**"), under which certain of the Company's and such Investors' obligations are conditioned upon the execution and delivery of this Agreement by such Investors, Existing Investors holding at least a majority in interest of the Registrable Securities (as defined in the Prior Agreement), and the Company;

WHEREAS, the undersigned Existing Investors hold at least a majority in interest of the Registrable Securities of the Company (as defined in the Prior Agreement); and

NOW, THEREFORE, in consideration of the mutual covenants contained herein and the consummation of the sale and purchase of shares of Series B Preferred Stock (as defined below) pursuant to the Purchase Agreement and the other valuation consideration, receipt of which is hereby acknowledged, the undersigned Existing Investors hereby agree that the Prior Agreement shall be amended and restated, and the parties to this Agreement further agree as follows:

1. Definitions.

For purposes of this Agreement:

1.1 “**Affiliate**” means, with respect to any specified Person, any other Person who or which, directly or indirectly, controls, is controlled by, or is under common control with such specified Person, including without limitation any general partner, officer, director, or manager of such Person and any venture capital fund or other investment fund now or hereafter existing that is controlled by one or more general partners or managing members of, or shares the same management company or investment adviser with, such Person.

1.2 **“Board of Directors”** means the Company’s Board of Directors.

1.3 **“Certificate of Incorporation”** means the Company’s Amended and Restated Certificate of Incorporation, as the same may be amended, restated or otherwise modified from time to time.

1.4 **“Common Stock”** means shares of the Company’s common stock, par value \$0.001 per share.

1.5 **“Damages”** means any loss, damage, claim or liability (joint or several) to which a party hereto may become subject under the Securities Act, the Exchange Act, or other federal or state law, insofar as such loss, damage, claim or liability (or any action in respect thereof) arises out of or is based upon (i) any untrue statement or alleged untrue statement of a material fact contained in any registration statement of the Company, including any preliminary prospectus or final prospectus contained therein or any amendments or supplements thereto; (ii) an omission or alleged omission to state therein a material fact required to be stated therein, or necessary to make the statements therein not misleading; or (iii) any violation or alleged violation by the indemnifying party (or any of its agents or Affiliates) of the Securities Act, the Exchange Act, any state securities law, or any rule or regulation promulgated under the Securities Act, the Exchange Act, or any state securities law.

1.6 **“Deemed Liquidation Event”** shall have the meaning given to such term in the Certificate of Incorporation.

1.7 **“Derivative Securities”** means any securities or rights convertible into, or exercisable or exchangeable for (in each case, directly or indirectly), Common Stock, including options and warrants.

1.8 **“Exchange Act”** means the Securities Exchange Act of 1934, as amended, and the rules and regulations promulgated thereunder.

1.9 **“Excluded Registration”** means (i) a registration relating to the sale of securities to employees of the Company or a subsidiary pursuant to a stock option, stock purchase, or similar plan; (ii) a registration relating to an SEC Rule 145 transaction; or (iii) a registration on any form that does not include substantially the same information as would be required to be included in a registration statement covering the sale of the Registrable Securities.

1.10 **“Fidelity”** shall mean Fidelity Management & Research Company and any successor or affiliated registered investment advisor to the Fidelity Investors.

1.11 **“Fidelity Investors”** shall mean any Investors advised or subadvised by Fidelity or one of its Affiliates.

1.12 **“Form S-1”** means such form under the Securities Act as in effect on the date hereof or any successor registration form under the Securities Act subsequently adopted by the SEC.

1.13 “**Form S-3**” means such form under the Securities Act as in effect on the date hereof or any registration form under the Securities Act subsequently adopted by the SEC that permits incorporation of substantial information by reference to other documents filed by the Company with the SEC.

1.14 “**GAAP**” means generally accepted accounting principles in the United States.

1.15 “**Holder**” means any holder of Registrable Securities who is a party to this Agreement.

1.16 “**Immediate Family Member**” means a child, stepchild, grandchild, parent, stepparent, grandparent, spouse, sibling, mother-in-law, father-in-law, son-in-law, daughter-in-law, brother-in-law, or sister-in-law, including adoptive relationships, of a natural person referred to herein.

1.17 “**Initiating Holders**” means, collectively, Holders who properly initiate a registration request under this Agreement.

1.18 “**Investor Directors**” means, collectively, the Series A Director and the Series B Director.

1.19 “**IPO**” means the Company’s first underwritten public offering of its Common Stock under the Securities Act.

1.20 “**Key Employee**” means any executive-level employee (including division director and vice president-level positions) as well as any employee who, either alone or in concert with others, develops, invents, programs, or designs any Company Intellectual Property (as defined in the Purchase Agreement).

1.21 “**Major Investor**” means any Investor that, individually or together with such Investor’s Affiliates, holds at least 750,000 shares of Registrable Securities (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization).

1.22 “**New Securities**” means, collectively, equity securities of the Company, whether or not currently authorized, as well as rights, options, or warrants to purchase such equity securities, or securities of any type whatsoever that are, or may become, convertible or exchangeable into or exercisable for such equity securities.

1.23 “**Person**” means any individual, corporation, partnership, trust, limited liability company, association or other entity.

1.24 “**Preferred Stock**” means the Series A Preferred Stock and the Series B Preferred Stock.

1.25 “**Registrable Securities**” means (i) the Common Stock issuable or issued upon conversion of the Preferred Stock; (ii) any Common Stock, or any Common Stock issued or

issuable (directly or indirectly) upon conversion and/or exercise of any other securities of the Company, held by the Investors or acquired by the Investors after the date hereof; and (iii) any Common Stock issued as (or issuable upon the conversion or exercise of any warrant, right, or other security that is issued as) a dividend or other distribution with respect to, or in exchange for or in replacement of, the shares referenced in clauses (i) and (ii) above; excluding in all cases, however, any Registrable Securities sold by a Person in a transaction in which the applicable rights under this Agreement are not assigned pursuant to Section 6.1, and excluding for purposes of Section 2 any shares for which registration rights have terminated pursuant to Section 2.13 of this Agreement.

1.26 “**Registrable Securities then outstanding**” means the number of shares at a point in time determined by adding the number of shares of outstanding Common Stock that are Registrable Securities at such time and the number of shares of Common Stock issuable (directly or indirectly) at such time pursuant to then exercisable and/or convertible securities that are Registrable Securities.

1.27 “**Restricted Securities**” means the securities of the Company required to bear the legend set forth in Section 2.12(b) hereof.

1.28 “**SEC**” means the Securities and Exchange Commission.

1.29 “**SEC Rule 144**” means Rule 144 promulgated by the SEC under the Securities Act, or any successor provisions.

1.30 “**SEC Rule 145**” means Rule 145 promulgated by the SEC under the Securities Act, or any successor provisions.

1.31 “**Securities Act**” means the Securities Act of 1933, as amended, and the rules and regulations promulgated thereunder.

1.32 “**Selling Expenses**” means all underwriting discounts, selling commissions, and stock transfer taxes applicable to the sale of Registrable Securities, and fees and disbursements of counsel for any Holder, except for the fees and disbursements of the Selling Holder Counsel borne and paid by the Company as provided in Section 2.6.

1.33 “**Selling Holder Counsel**” shall have the meaning assigned to it in Section 2.6.

1.34 “**Series A Director**” means the director of the Company that has been solely elected or designated by the holders of record of the Series A Preferred Stock pursuant to the Certificate of Incorporation, the Stockholders Agreement or otherwise.

1.35 “**Series A Preferred Stock**” means shares of the Company’s Series A Preferred Stock, par value \$0.001 per share.

1.36 “**Series B Director**” means the director of the Company that has been solely elected or designated by the holders of record of the Series B Preferred Stock pursuant to the Certificate of Incorporation, the Stockholders Agreement or otherwise.

1.37 “**Series B Preferred Stock**” means shares of the Company’s Series B Preferred Stock, par value \$0.001 per share.

1.38 “**Stockholders Agreement**” means the Amended and Restated Stockholders Agreement dated as of the date hereof, by and among the Company, the Investors, and Key Holders (as defined therein), as the same may be amended, restated or otherwise modified from time to time.

2. Registration Rights. The Company covenants and agrees as follows:

2.1 Demand Registration.

(a) Form S-1 Demand. Beginning upon the earlier of (i) five (5) years after the date of this Agreement or (ii) six (6) months after the effective date of the registration statement for the IPO, if the Company receives a request from Holders of at least forty percent (40%) of the Registrable Securities then outstanding that the Company file a Form S-1 registration statement with respect to at least forty percent (40%) of the Registrable Securities then outstanding, having the anticipated aggregate offering amount of at least \$5.0 million, then the Company shall (x) within ten (10) days after the date such request is given, give notice thereof (the “**Demand Notice**”) to all Holders other than the Initiating Holders; and (y) as soon as practicable, and in any event within sixty (60) days after the date such request is given by the Initiating Holders, file a Form S-1 registration statement under the Securities Act covering all Registrable Securities that the Initiating Holders requested to be registered and any additional Registrable Securities requested to be included in such registration by any other Holders, as specified by notice given by each such Holder to the Company within twenty (20) days after the date the Demand Notice is given, and in each case, subject to the limitations of Section 2.1(c) and Section 2.3.

(b) Form S-3 Demand. If at any time when it is eligible to use a Form S-3 registration statement, the Company receives a request from Holders of at least twenty-five percent (25%) of the Registrable Securities then outstanding that the Company file a Form S-3 registration statement with respect to outstanding Registrable Securities of such Holders having an anticipated aggregate offering amount, net of Selling Expenses, of at least \$3.0 million, then the Company shall (i) within ten (10) days after the date such request is given, give a Demand Notice to all Holders other than the Initiating Holders; and (ii) as soon as practicable, and in any event within forty-five (45) days after the date such request is given by the Initiating Holders, file a Form S-3 registration statement under the Securities Act covering all Registrable Securities requested to be included in such registration by any other Holders, as specified by notice given by each such Holder to the Company within twenty (20) days of the date the Demand Notice is given, and in each case, subject to the limitations of Section 2.1(c) and Section 2.3.

(c) Notwithstanding the foregoing obligations, if the Company furnishes to Holders requesting a registration pursuant to this Section 2.1 a certificate signed by the Company’s chief executive officer or other most senior executive officer then in office stating that in the good faith judgment of the Board of Directors it would be materially detrimental to the Company and its stockholders for such registration statement to either become

effective or remain effective for as long as such registration statement otherwise would be required to remain effective, because such action would (i) materially interfere with a significant acquisition, corporate reorganization, or other similar transaction involving the Company; (ii) require premature disclosure of material information that the Company has a bona fide business purpose for preserving as confidential; or (iii) render the Company unable to comply with requirements under the Securities Act or Exchange Act, then the Company shall have the right to defer taking action with respect to such filing, and any time periods with respect to filing or effectiveness thereof shall be tolled correspondingly, for a period of not more than one hundred twenty (120) days after the request of the Initiating Holders is given; provided, however, that the Company may not invoke this right more than once in any twelve (12) month period, nor shall the Company invoke this right more than twice in all periods; and provided further that the Company shall not register any securities for its own account or that of any other stockholder during either one hundred twenty (120) day period other than an Excluded Registration.

(d) The Company shall not be obligated to effect, or to take any action to effect, any registration pursuant to Section 2.1(a) (i) if it delivers notice to the Holders within thirty (30) days after any registration request of its intent to file a registration statement for a public offering within ninety (90) days; (ii) during the period that is one hundred eighty (180) days after commencing a Company-initiated registration; (iii) after the Company has effected two (2) registrations pursuant to Section 2.1(a); or (iv) if the Initiating Holders propose to dispose of shares of Registrable Securities that may be immediately registered on Form S-3 pursuant to a request made pursuant to Section 2.1(b). The Company shall not be obligated to effect, or to take any action to effect, any registration pursuant to Section 2.1(b) if the Company has effected two (2) registrations pursuant to Section 2.1(b) within the twelve (12) month period immediately preceding the date of such request. A registration shall not be counted as “effected” for purposes of this Section 2.1(d) until such time as the applicable registration statement has been declared effective by the SEC, unless the Initiating Holders withdraw their request for such registration (other than as a result of a material adverse change to the Company), elect not to pay the registration expenses therefor, and forfeit their right to one demand registration statement pursuant to Section 2.6, in which case such withdrawn registration statement shall be counted as “effected” for purposes of this Section 2.1(d).

2.2 Company Registration. If the Company proposes to register (including, for this purpose, a registration effected by the Company for stockholders other than the Holders) any of its Common Stock under the Securities Act in connection with the public offering of such securities solely for cash (other than in an Excluded Registration), the Company shall, at such time, promptly give each Holder notice of such registration. Upon the request of each Holder given within twenty (20) days after such notice is given by the Company, the Company shall, subject to the provisions of Section 2.3, cause to be registered all of the Registrable Securities that each such Holder has requested to be included in such registration. The Company shall have the right to terminate or withdraw any registration initiated by it under this Section 2.2 before the effective date of such registration, whether or not any Holder has elected to include Registrable Securities in such registration. The expenses (other than Selling Expenses) of such withdrawn registration shall be borne by the Company in accordance with Section 2.6.

2.3 Underwriting Requirements.

(a) If, pursuant to Section 2.1, the Initiating Holders intend to distribute the Registrable Securities covered by their request by means of an underwriting, they shall so advise the Company as a part of their request made pursuant to Section 2.1, and the Company shall include such information in the Demand Notice. The underwriter(s) will be selected by the Company and shall be reasonably acceptable to a majority-in-interest of the Initiating Holders. In such event, the right of any Holder to include such Holder's Registrable Securities in such registration shall be conditioned upon such Holder's participation in such underwriting and the inclusion of such Holder's Registrable Securities in the underwriting to the extent provided herein. All Holders proposing to distribute their securities through such underwriting shall (together with the Company as provided in Section 2.4(e)) enter into an underwriting agreement in customary form with the underwriter(s) selected for such underwriting. Notwithstanding any other provision of this Section 2.3, if the managing underwriter(s) advise the Initiating Holders in writing that marketing factors require a limitation on the number of shares to be underwritten, then the Initiating Holders shall so advise all Holders that otherwise would be underwritten pursuant hereto, and the number of Registrable Securities that may be included in the underwriting shall be allocated among such Holders, including the Initiating Holders, in proportion (as nearly as practicable) to the number of Registrable Securities owned by each, or in such other proportion as shall mutually be agreed to by all such selling Holders; provided, however, that the number of Registrable Securities held by the Holders to be included in such underwriting shall not be reduced unless all other securities are first entirely excluded from the underwriting. To facilitate the allocation of shares in accordance with the above provisions, the Company or the underwriters may round the number of shares allocated to any Holder to the nearest 100 shares.

(b) In connection with any offering involving an underwriting of shares of the Company's capital stock pursuant to Section 2.2, the Company shall not be required to include any of the Registrable Securities in such underwriting unless the Holders accept the terms of the underwriting as agreed upon between the Company and its underwriters, and then only in such quantity as the underwriters in their sole discretion determine will not jeopardize the success of the offering by the Company. If the total number of securities, including Registrable Securities, requested by Holders to be included in such offering exceeds the number of securities to be sold (other than by the Company) that the underwriters in their reasonable discretion determine is compatible with the success of the offering, then the Company shall be required to include in the offering only that number of such securities, including Registrable Securities, which the underwriters and the Company in their sole discretion determine will not jeopardize the success of the offering. If the underwriters determine that less than all of the Registrable Securities requested to be registered can be included in such offering, then the Registrable Securities that are included in such offering shall be allocated among the selling Holders in proportion (as nearly as practicable to) the number of Registrable Securities owned by each selling Holder or in such other proportions as shall mutually be agreed to by all such selling Holders. To facilitate the allocation of shares in accordance with the above provisions, the Company or the underwriters may round the number of shares allocated to any Holder to the nearest 100 shares. Notwithstanding the foregoing, in no event shall (i) the number of Registrable Securities included in the offering be reduced unless all other securities (other than securities to be sold by the Company) are first entirely excluded from the offering, or (ii) the

number of Registrable Securities included in the offering be reduced below thirty percent (30%) of the total number of securities included in such offering, unless such offering is the IPO, in which case the selling Holders may be excluded further if the underwriters make the determination described above and no other stockholder's securities are included in such offering. For purposes of the provision in this Section 2.3(b) concerning apportionment, for any selling Holder that is a partnership, limited liability company, or corporation, the partners, members, retired partners, retired members, stockholders, and Affiliates of such Holder, or the estates and Immediate Family Members of any such partners, retired partners, members, and retired members and any trusts for the benefit of any of the foregoing Persons, shall be deemed to be a single "selling Holder," and any pro rata reduction with respect to such "selling Holder" shall be based upon the aggregate number of Registrable Securities owned by all Persons included in such "selling Holder," as defined in this sentence.

(c) For purposes of Section 2.1, a registration shall not be counted as "effected" if, as a result of an exercise of the underwriter's cutback provisions in Section 2.3(a) and (b), less than the total number of Registrable Securities that Holders have requested to be included in such registration statement are actually included.

2.4 Obligations of the Company.

Whenever required under this Section 2 to effect the registration of any Registrable Securities, the Company shall, as expeditiously as reasonably possible:

(a) prepare and file with the SEC a registration statement with respect to such Registrable Securities and use its commercially reasonable efforts to cause such registration statement to become effective and, upon the request of the Holders of at least 65% of the Registrable Securities registered thereunder, keep such registration statement effective for a period of up to one hundred twenty (120) days or, if earlier, until the distribution contemplated in the registration statement has been completed; provided, however, that (i) such one hundred twenty (120) day period shall be extended for a period of time equal to the period the Holder refrains, at the request of an underwriter of the Company, from selling any securities included in such registration, and (ii) in the case of any registration of Registrable Securities on Form S-3 that are intended to be offered on a continuous or delayed basis, subject to compliance with applicable SEC rules, such one hundred twenty (120) day period shall be extended for up to one hundred eighty (180) days, if necessary, to keep the registration statement effective until all such Registrable Securities are sold;

(b) prepare and file with the SEC such amendments and supplements to such registration statement, and the prospectus used in connection with such registration statement, as may be necessary to comply with the Securities Act in order to enable the disposition of all securities covered by such registration statement;

(c) furnish to the selling Holders such numbers of copies of a prospectus, including a preliminary prospectus, as required by the Securities Act, and such other documents as the Holders may reasonably request in order to facilitate their disposition of their Registrable Securities;

(d) use its commercially reasonable efforts to register and qualify the securities covered by such registration statement under such other securities or blue-sky laws of such jurisdictions as shall be reasonably requested by the selling Holders; provided that the Company shall not be required to qualify to do business or to file a general consent to service of process in any such states or jurisdictions, unless the Company is already subject to service in such jurisdiction and except as may be required by the Securities Act;

(e) in the event of any underwritten public offering, enter into and perform its obligations under an underwriting agreement, in usual and customary form, with the underwriter(s) of such offering;

(f) use its commercially reasonable efforts to cause all such Registrable Securities covered by such registration statement to be listed on a national securities exchange or trading system and each securities exchange and trading system (if any) on which similar securities issued by the Company are then listed;

(g) provide a transfer agent and registrar for all Registrable Securities registered pursuant to this Agreement and provide a CUSIP number for all such Registrable Securities, in each case not later than the effective date of such registration;

(h) promptly make available for inspection by the selling Holders, any underwriter(s) participating in any disposition pursuant to such registration statement, and any attorney or accountant or other agent retained by any such underwriter or selected by the selling Holders, all financial and other records, pertinent corporate documents, and properties of the Company, and cause the Company's officers, directors, employees, and independent accountants to supply all information reasonably requested by any such seller, underwriter, attorney, accountant, or agent, in each case, as necessary or advisable to verify the accuracy of the information in such registration statement and to conduct appropriate due diligence in connection therewith;

(i) notify each selling Holder, promptly after the Company receives notice thereof, of the time when such registration statement has been declared effective or a supplement to any prospectus forming a part of such registration statement has been filed; and

(j) after such registration statement becomes effective, notify each selling Holder of any request by the SEC that the Company amend or supplement such registration statement or prospectus.

2.5 Furnish Information. It shall be a condition precedent to the obligations of the Company to take any action pursuant to this Section 2 with respect to the Registrable Securities of any selling Holder that such Holder shall furnish to the Company such information regarding itself, the Registrable Securities held by it, and the intended method of disposition of such securities as is reasonably required to effect the registration of such Holder's Registrable Securities.

2.6 Expenses of Registration. All expenses (other than Selling Expenses) incurred in connection with registrations, filings, or qualifications pursuant to Section 2, including all registration, filing, and qualification fees; printers' and accounting fees; fees and

disbursements of counsel for the Company; and the reasonable fees and disbursements of one counsel for the selling Holders (“**Selling Holder Counsel**”) selected by the Holders of at least 65% of the Registrable Securities, shall be borne and paid by the Company; provided, however, that the Company shall not be required to pay for any expenses of any registration proceeding begun pursuant to Section 2.1 if the registration request is subsequently withdrawn at the request of the Holders of at least 65% of the Registrable Securities to be registered (in which case all selling Holders shall bear such expenses pro rata based upon the number of Registrable Securities that were to be included in the withdrawn registration), unless the Holders of at least 65% of the Registrable Securities agree to forfeit their right to one registration pursuant to Section 2.1(a) or Section 2.1(b), as the case may be; provided further that if, at the time of such withdrawal, the Holders have learned of a material adverse change in the condition, business, or prospects of the Company from that known to the Holders at the time of their request and have withdrawn the request with reasonable promptness after learning of such information, then the Holders shall not be required to pay any of such expenses and shall not forfeit their right to one registration pursuant to Section 2.1(a) or Section 2.1(b). All Selling Expenses relating to Registrable Securities registered pursuant to this Section 2 shall be borne and paid by the Holders pro rata on the basis of the number of Registrable Securities registered on their behalf.

2.7 Delay of Registration. No Holder shall have any right to obtain or seek an injunction restraining or otherwise delaying any registration pursuant to this Agreement as the result of any controversy that might arise with respect to the interpretation or implementation of this Section 2.

2.8 Indemnification. If any Registrable Securities are included in a registration statement under this Section 2:

(a) To the extent permitted by law, the Company will indemnify and hold harmless each selling Holder, and the partners, members, officers, directors, and stockholders of each such Holder; legal counsel, accountants and investment advisers for each such Holder; any underwriter (as defined in the Securities Act) for each such Holder; and each Person, if any, who controls such Holder or underwriter within the meaning of the Securities Act or the Exchange Act, against any Damages, and the Company will pay to each such Holder, underwriter, controlling Person, or other aforementioned Person any legal or other expenses reasonably incurred thereby in connection with investigating or defending any claim or proceeding from which Damages may result, as such expenses are incurred; provided, however, that the indemnity agreement contained in this Section 2.8(a) shall not apply to amounts paid in settlement of any such claim or proceeding if such settlement is effected without the consent of the Company, which consent shall not be unreasonably withheld, nor shall the Company be liable for any Damages to the extent that they arise out of or are based upon actions or omissions made in reliance upon and in conformity with written information furnished by or on behalf of any such Holder, underwriter, controlling Person, or other aforementioned Person expressly for use in connection with such registration.

(b) To the extent permitted by law, each selling Holder, severally and not jointly, will indemnify and hold harmless the Company, and each of its directors, each of its officers who has signed the registration statement, each Person (if any), who controls the Company within the meaning of the Securities Act, legal counsel and accountants for the

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Company, any underwriter (as defined in the Securities Act), any other Holder selling securities in such registration statement, and any controlling Person of any such underwriter or other Holder, against any Damages, in each case only to the extent that such Damages arise out of or are based upon actions or omissions made in reliance upon and in conformity with written information furnished by or on behalf of such selling Holder expressly for use in connection with such registration; and each such selling Holder will pay to the Company and each other aforementioned Person any legal or other expenses reasonably incurred thereby in connection with investigating or defending any claim or proceeding from which Damages may result, as such expenses are incurred; provided, however, that the indemnity agreement contained in this Section 2.8(b) shall not apply to amounts paid in settlement of any such claim or proceeding if such settlement is effected without the consent of the Holder, which consent shall not be unreasonably withheld; and provided further that in no event shall the aggregate amounts payable by any Holder by way of indemnity or contribution under this Section 2.8(b) and Section 2.8(d) exceed the proceeds from the offering received by such Holder (net of any Selling Expenses paid by such Holder), except in the case of fraud or willful misconduct by such Holder.

(c) Promptly after receipt by an indemnified party under this Section 2.8 of notice of the commencement of any action (including any governmental action) for which a party may be entitled to indemnification hereunder, such indemnified party will, if a claim in respect thereof is to be made against any indemnifying party under this Section 2.8, give the indemnifying party notice of the commencement thereof. The indemnifying party shall have the right to participate in such action and, to the extent the indemnifying party so desires, participate jointly with any other indemnifying party to which notice has been given, and to assume the defense thereof with counsel mutually satisfactory to the parties; provided, however, that an indemnified party (together with all other indemnified parties that may be represented without conflict by one counsel) shall have the right to retain one separate counsel, with the fees and expenses to be paid by the indemnifying party, if representation of such indemnified party by the counsel retained by the indemnifying party would be inappropriate due to actual or potential differing interests between such indemnified party and any other party represented by such counsel in such action. The failure to give notice to the indemnifying party within a reasonable time of the commencement of any such action shall relieve such indemnifying party of any liability to the indemnified party under this Section 2.8, to the extent that such failure materially prejudices the indemnifying party’s ability to defend such action. The failure to give notice to the indemnifying party will not relieve it of any liability that it may have to any indemnified party otherwise than under this Section 2.8.

(d) To provide for just and equitable contribution to joint liability under the Securities Act in any case in which either (i) any party otherwise entitled to indemnification hereunder makes a claim for indemnification pursuant to this Section 2.8 but it is judicially determined (by the entry of a final judgment or decree by a court of competent jurisdiction and the expiration of time to appeal or the denial of the last right of appeal) that such indemnification may not be enforced in such case, notwithstanding the fact that this Section 2.8 provides for indemnification in such case, or (ii) contribution under the Securities Act may be required on the part of any party hereto for which indemnification is provided under this Section 2.8, then, and in each such case, such parties will contribute to the aggregate losses, claims, damages, liabilities, or expenses to which they may be subject (after contribution from others) in such proportion as is appropriate to reflect the relative fault of each of the

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indemnifying party and the indemnified party in connection with the statements, omissions, or other actions that resulted in such loss, claim, damage, liability, or expense, as well as to reflect any other relevant equitable considerations. The relative fault of the indemnifying party and of the indemnified party shall be determined by reference to, among other things, whether the untrue or allegedly untrue statement of a material fact, or the omission or alleged omission of a material fact, relates to information supplied by the indemnifying party or by the indemnified party and the parties' relative intent, knowledge, access to information, and opportunity to correct or prevent such statement or omission; provided, however, that, in any such case, (x) no Holder will be required to contribute any amount in excess of the public offering price of all such Registrable Securities offered and sold by such Holder pursuant to such registration statement, and (y) no Person guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the Securities Act) will be entitled to contribution from any Person who was not guilty of such fraudulent misrepresentation; and provided further that in no event shall a Holder's liability pursuant to this Section 2.8(d), when combined with the amounts paid or payable by such Holder pursuant to Section 2.8(b), exceed the proceeds from the offering received by such Holder (net of any Selling Expenses paid by such Holder), except in the case of willful misconduct or fraud by such Holder.

(e) Notwithstanding the foregoing, to the extent that the provisions on indemnification and contribution contained in the underwriting agreement entered into in connection with the underwritten public offering are in conflict with the foregoing provisions, the provisions in the underwriting agreement shall control.

(f) Unless otherwise superseded by an underwriting agreement entered into in connection with the underwritten public offering, the obligations of the Company and Holders under this Section 2.8 shall survive the completion of any offering of Registrable Securities in a registration under this Section 2, and otherwise shall survive the termination of this Agreement.

2.9 Reports Under Exchange Act. With a view to making available to the Holders the benefits of SEC Rule 144 and any other rule or regulation of the SEC that may at any time permit a Holder to sell securities of the Company to the public without registration or pursuant to a registration on Form S-3, the Company shall:

(a) make and keep available adequate current public information, as those terms are understood and defined in SEC Rule 144, at all times after the effective date of the registration statement filed by the Company for the IPO;

(b) use commercially reasonable efforts to file with the SEC in a timely manner all reports and other documents required of the Company under the Securities Act and the Exchange Act (at any time after the Company has become subject to such reporting requirements); and

(c) furnish to any Holder, so long as the Holder owns any Registrable Securities, forthwith upon request (i) to the extent accurate, a written statement by the Company that it has complied with the reporting requirements of SEC Rule 144 (at any time after ninety (90) days after the effective date of the registration statement filed by the Company for the IPO),

the Securities Act, and the Exchange Act (at any time after the Company has become subject to such reporting requirements), or that it qualifies as a registrant whose securities may be resold pursuant to Form S-3 (at any time after the Company so qualifies); (ii) a copy of the most recent annual or quarterly report of the Company and such other reports and documents so filed by the Company; and (iii) such other information as may be reasonably requested in availing any Holder of any rule or regulation of the SEC that permits the selling of any such securities without registration (at any time after the Company has become subject to the reporting requirements under the Exchange Act) or pursuant to Form S-3 (at any time after the Company so qualifies to use such form).

2.10 Limitations on Subsequent Registration Rights. From and after the date of this Agreement, the Company shall not, without the prior written consent of the Holders of at least 65% in interest of the Registrable Securities then outstanding (the “**Requisite Vote**”), enter into any agreement with any holder or prospective holder of any securities of the Company that would allow such holder or prospective holder (i) to include such securities in any registration unless, under the terms of such agreement, such holder or prospective holder may include such securities in any such registration only to the extent that the inclusion of such securities will not reduce the number of the Registrable Securities of the Holders that are included or (ii) to demand registration of any securities held by such holder or prospective holder; provided that this limitation shall not apply to any additional Investor who becomes a party to this Agreement in accordance with Section 6.9.

2.11 “Market Stand-off” Agreement. Each Holder hereby agrees that, if required by the managing underwriter, it will not, during the period commencing on the date of the final prospectus relating to the IPO and ending on the date specified by the Company and the managing underwriter (such period not to exceed one hundred eighty (180) days, which period may be extended upon the request of the managing underwriter for such longer period of time as is necessary to enable such underwriter to issue a research report or to make a public appearance that relates to an earnings release or announcement by the Company within fifteen (15) days prior to or after the day that is one hundred eighty (180) days after the effective date of the registration statement relating to such offering, but in any event not to exceed two hundred ten (210) days following the effective date of the registration statement relating to such offering), (i) lend; offer; pledge; sell; contract to sell; sell any option or contract to purchase; purchase any option or contract to sell; grant any option, right, or warrant to purchase; or otherwise transfer or dispose of, directly or indirectly, any shares of Common Stock or any securities convertible into or exercisable or exchangeable (directly or indirectly) for Common Stock held immediately before the effective date of the registration statement for the IPO or (ii) enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of such securities, whether any such transaction described in clause (i) or (ii) above is to be settled by delivery of Common Stock or other securities, in cash, or otherwise. The foregoing provisions of this Section 2.11 (A) shall apply only to the IPO, (B) shall not apply to the sale of shares of Common Stock acquired in the IPO or in the open market following the IPO, (C) shall not apply to the sale of any shares to an underwriter pursuant to an underwriting agreement, and (D) shall be applicable to the Holders only if all officers, directors, and stockholders individually owning more than one percent (1%) of the Company’s outstanding Common Stock (after giving effect to conversion into Common Stock of all outstanding Preferred Stock) are subject to the same restrictions. The underwriters in connection with such

registration are intended third-party beneficiaries of this Section 2.11 and shall have the right, power, and authority to enforce the provisions hereof as though they were a party hereto. Each Holder further agrees to execute such agreements as may be reasonably requested by the underwriters in connection with such registration that are consistent with this Section 2.11 or that are necessary to give further effect thereto. The Company agrees to use its reasonable efforts to obtain the agreement of the managing underwriter to periodic early releases of portions of the securities subject to such lock-up agreements upon the request of a Holder to such early release, provided that in the event of any early release, all Holders will be released on a pro rata basis from such agreements. If any of the obligations described in this Section 2.11 are waived or terminated with respect to any of the securities of any such Holder, officer, director or greater than one-percent stockholder (in any such case, the "Released Securities"), the foregoing provisions shall be waived or terminated, as applicable, to the same extent and with respect to the same percentage of securities of each Holder as the percentage of Released Securities represent with respect to the securities held by the applicable Holder, officer, director or greater than one-percent stockholder

2.12 Restrictions on Transfer.

(a) The Preferred Stock and the Registrable Securities shall not be sold, pledged, or otherwise transferred, and the Company shall not recognize any such sale, pledge, or transfer, except upon the conditions specified in this Agreement, which conditions are intended to ensure compliance with the provisions of the Securities Act. A transferring Holder will cause any proposed purchaser, pledgee, or transferee of the Preferred Stock and the Registrable Securities held by such Holder to agree to take and hold such securities subject to the provisions and upon the conditions specified in this Agreement. Notwithstanding the foregoing, the Company shall not require any transferee of shares pursuant to an effective registration statement or, following the IPO, SEC Rule 144, in each case, to be bound by the terms of this Agreement.

(b) Each certificate or instrument representing (i) the Preferred Stock, (ii) the Registrable Securities, and (iii) any other securities issued in respect of the securities referenced in clauses (i) and (ii), upon any stock split, stock dividend, recapitalization, merger, consolidation, or similar event, shall (unless otherwise permitted by the provisions of Section 2.12(c)) be stamped or otherwise imprinted with a legend substantially in the following form:

THE SECURITIES REPRESENTED HEREBY HAVE BEEN ACQUIRED FOR INVESTMENT AND HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED. SUCH SHARES MAY NOT BE SOLD, PLEDGED, OR TRANSFERRED IN THE ABSENCE OF SUCH REGISTRATION OR A VALID EXEMPTION FROM THE REGISTRATION AND PROSPECTUS DELIVERY REQUIREMENTS OF SAID ACT.

THE SECURITIES REPRESENTED HEREBY MAY BE TRANSFERRED ONLY IN ACCORDANCE WITH THE TERMS OF AN AGREEMENT BETWEEN THE COMPANY AND THE STOCKHOLDER, A COPY OF WHICH IS ON FILE WITH THE SECRETARY OF THE COMPANY.

The Holders consent to the Company making a notation in its records and giving instructions to any transfer agent of the Restricted Securities in order to implement the restrictions on transfer set forth in this Section 2.12.

(c) The holder of each certificate representing Restricted Securities, by acceptance thereof, agrees to comply in all respects with the provisions of this Section 2. Before any proposed sale, pledge, or transfer of any Restricted Securities, unless there is in effect a registration statement under the Securities Act covering the proposed transaction, or, following the IPO, the transfer is made pursuant to SEC Rule 144 the Holder thereof shall give notice to the Company of such Holder's intention to effect such sale, pledge, or transfer. Each such notice shall describe the manner and circumstances of the proposed sale, pledge, or transfer in sufficient detail and, if reasonably requested by the Company, shall be accompanied at such Holder's expense by either (i) a written opinion of legal counsel who shall, and whose legal opinion shall, be reasonably satisfactory to the Company, addressed to the Company, to the effect that the proposed transaction may be effected without registration under the Securities Act; (ii) a "no action" letter from the SEC to the effect that the proposed sale, pledge, or transfer of such Restricted Securities without registration will not result in a recommendation by the staff of the SEC that action be taken with respect thereto; or (iii) any other evidence reasonably satisfactory to counsel to the Company to the effect that the proposed sale, pledge, or transfer of the Restricted Securities may be effected without registration under the Securities Act, whereupon the Holder of such Restricted Securities shall be entitled to sell, pledge, or transfer such Restricted Securities in accordance with the terms of the notice given by the Holder to the Company. The Company will not require such a legal opinion or "no action" letter (x) in any transaction in compliance with SEC Rule 144 or (y) in any transaction in which such Holder distributes Restricted Securities to an Affiliate of such Holder for no consideration; provided that, with respect to transfers under the foregoing clause (y), each transferee agrees in writing to be subject to the terms of this Section 2.12. Each certificate or instrument evidencing the Restricted Securities transferred as above provided shall bear, except if such transfer is made pursuant to SEC Rule 144 or pursuant to an effective registration statement, the appropriate restrictive legend set forth in Section 2.12(b), except that such certificate shall not bear such restrictive legend if, in the opinion of counsel for such Holder and the Company, such legend is not required in order to establish compliance with any provisions of the Securities Act.

2.13 Termination of Registration Rights. The right of any Holder to request registration or inclusion of Registrable Securities in any registration pursuant to Section 2.1 or Section 2.2 shall terminate upon the earliest to occur of:

- (a) the closing of a Deemed Liquidation Event, as such term is defined in the Certificate of Incorporation;
- (b) following the IPO, such time as Rule 144 or another similar exemption under the Securities Act is available for the sale of all of such Holder's shares without limitation during a three-month period without registration; and
- (c) the fifth (5th) anniversary of the IPO.

3. Information and Observer Rights.

3.1 Delivery of Financial Statements. The Company shall deliver to each Major Investor the required items listed below, except that the Company shall deliver to all Investors the items required by Sections 3.1(b) and (c):

(a) as soon as practicable, but in any event within ninety (90) days after the end of each fiscal year of the Company, unaudited statements of income and of cash flows for such fiscal year, and an unaudited balance sheet and a statement of stockholders' equity as of the end of such fiscal year, all prepared in accordance with GAAP (except that such financial statements may (i) be subject to normal year-end audit adjustments and (ii) not contain all notes thereto that may be required in accordance with GAAP);

(b) as soon as practicable, but in any event within one hundred twenty (120) days after the end of each fiscal year of the Company, (i) a balance sheet as of the end of such year, (ii) statements of income and of cash flows for such year, and (iii) a statement of stockholders' equity as of the end of such year, all such financial statements audited and certified by independent public accountants of nationally or regionally recognized standing selected by the Company and approved by the Board of Directors;

(c) as soon as practicable but in any event within forty-five (45) days after the end of each of the first three (3) quarters of each fiscal year of the Company, unaudited statements of income and of cash flows for such fiscal quarter, and an unaudited balance sheet and a statement of stockholders' equity as of the end of such fiscal quarter, all prepared in accordance with GAAP (except that such financial statements may (i) be subject to normal year-end audit adjustments and (ii) not contain all notes thereto that may be required in accordance with GAAP);

(d) as soon as practicable, but in any event within thirty (30) days after the end of each month, an unaudited income statement and statement of cash flows for such month, and an unaudited balance sheet and statement of stockholders' equity as of the end of such month, all prepared in accordance with GAAP (except that such financial statements may (i) be subject to normal year-end audit adjustments and (ii) not contain all notes thereto that may be required in accordance with GAAP);

(e) as soon as practicable, but in any event within forty-five (45) days after the end of each of the first three (3) quarters of each fiscal year of the Company, a statement showing the number of shares of each class and series of capital stock and securities convertible into or exercisable for shares of capital stock outstanding at the end of the period, the Common Stock issuable upon conversion or exercise of any outstanding securities convertible or exercisable for Common Stock and the exchange ratio or exercise price applicable thereto, and the number of shares of issued stock options and stock options not yet issued but reserved for issuance, if any, all in sufficient detail as to permit each Major Investor to calculate their respective percentage equity ownership in the Company, and certified by the chief financial officer or chief executive officer of the Company as being true, complete, and correct.

(f) as soon as practicable, but in any event thirty (30) days before the end of each fiscal year, a budget and business plan for the next fiscal year (collectively, the “**Budget**”), approved by the Board of Directors and prepared on a monthly basis, including balance sheets, income statements, and statements of cash flow for such months and, promptly after prepared, any other budgets or revised budgets prepared by the Company; and

(g) such other information relating to the financial condition, business, prospects, or corporate affairs of the Company as any Major Investor may from time to time reasonably request; provided, however, that the Company shall not be obligated under this Section 3.1 to provide information (i) that the Company reasonably determines in good faith to be a trade secret or confidential information or (ii) the disclosure of which would adversely affect the attorney-client privilege between the Company and its counsel.

If, for any period, the Company has any subsidiary whose accounts are consolidated with those of the Company, then in respect of such period the financial statements delivered pursuant to the foregoing sections shall be the consolidated and consolidating financial statements of the Company and all such consolidated subsidiaries.

Notwithstanding anything else in this Section 3.1 to the contrary, the Company may cease providing the information set forth in this Section 3.1 during the period starting with the date thirty (30) days before the Company’s good-faith estimate of the date of filing of a registration statement if it reasonably concludes it must do so to comply with the SEC rules applicable to such registration statement and related offering; provided that the Company’s covenants under this Section 3.1 shall be reinstated at such time as the Company is no longer actively employing its commercially reasonable efforts to cause such registration statement to become effective.

3.2 Inspection. The Company shall permit each Major Investor, at such Major Investor’s expense, to visit and inspect the Company’s properties; examine its books of account and records; and discuss the Company’s affairs, finances, and accounts with its officers, during normal business hours of the Company as may be reasonably requested by the Major Investor; provided, however, that the Company shall not be obligated pursuant to this Section 2 to provide access to any information that it reasonably considers to be a trade secret or confidential information or the disclosure of which would adversely affect the attorney-client privilege between the Company and its counsel.

3.3 Observer Rights. As long as Aventis Inc. (“Aventis”) continues to own not less than fifty percent (50%) of the shares of the Series B Preferred Stock it is purchasing under the Purchase Agreement (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization) (or an equivalent amount of Common Stock issued upon conversion thereof), the Company shall invite one representative of Aventis to attend all meetings of the Board of Directors in a nonvoting observer capacity (the “Aventis Observer”). As long as Casdin Partners Master Fund L.P. (“Casdin”) continues to own not less than fifty percent (50%) of the shares of the Series B Preferred Stock it is purchasing under the Purchase Agreement (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization) (or an equivalent amount of Common Stock issued upon conversion thereof), the Company shall invite one representative of Casdin to attend all meetings of the Board of Directors in a nonvoting observer capacity (the

“Casdin Observer”). As long as 6 Dimensions Capital L.P. and 6 Dimensions Affiliates Fund, L.P. (together, “6 Dimensions”) continue to own in the aggregate not less than fifty percent (50%) of the shares of the Series B Preferred Stock 6 Dimensions is purchasing under the Purchase Agreement (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization) (or an equivalent amount of Common Stock issued upon conversion thereof), the Company shall invite one representative of 6 Dimensions to attend all meetings of the Board of Directors in a nonvoting observer capacity (the “6 Dimensions Observer”, and, together with the Aventis Observer and the Casdin Observer, the “Board Observers”). The Company shall give to each Board Observer copies of all notices, minutes, consents, and other materials that it provides to its directors at the same time and in the same manner as provided to such directors; provided, however, that each Board Observer shall agree to hold in confidence and trust and to act in a fiduciary manner with respect to all information so provided; and provided further, that the Company reserves the right to withhold any information and to exclude a Board Observer from any meeting or portion thereof if access to such information or attendance at such meeting could adversely affect the attorney-client privilege between the Company and its counsel or result in disclosure of trade secrets or a conflict of interest.

3.4 Termination of Information Rights. The covenants set forth in Sections 3.1, 3.2 and 3.3 shall terminate and be of no further force or effect upon the earliest to occur of (i) immediately before, but subject to, the consummation of the IPO, (ii) when the Company first becomes subject to the periodic reporting requirements of Section 12(g) or 15(d) of the Exchange Act, or (iii) upon a Deemed Liquidation Event; provided, that, with respect to clause (iii), the covenants set forth in Section 3.1 shall only terminate if the consideration received by the Investors in such Deemed Liquidation Event is in the form of cash and/or publicly traded securities unless the Investors receive financial information from the acquiring company or other successor to the Company comparable to those set forth in Section 3.1.

3.5 Confidentiality. Each Investor agrees that such Investor will keep confidential and will not disclose, divulge, or use for any purpose (other than to monitor its investment in the Company) any confidential information obtained from the Company pursuant to the terms of this Agreement (including notice of the Company’s intention to file a registration statement), unless such confidential information (a) is known or becomes known to the public in general (other than as a result of a breach of this Section 3.5 by such Investor), (b) is or has been independently developed or conceived by the Investor without use of the Company’s confidential information, or (c) is or has been made known or disclosed to the Investor by a third party without a breach of any obligation of confidentiality such third party may have to the Company; provided, however, that an Investor may disclose confidential information (i) to its attorneys, accountants, consultants, and other professionals to the extent necessary to obtain their services in connection with monitoring its investment in the Company; (ii) to any prospective purchaser of any Registrable Securities from such Investor, if such prospective purchaser agrees to be bound by the provisions of this Section 3.5; (iii) to any existing or prospective Affiliate, partner, member, stockholder, or wholly owned subsidiary of such Investor in the ordinary course of business, provided that such Investor informs such Person that such information is confidential and directs such Person to maintain the confidentiality of such information; or (iv) as may otherwise be required by law, provided that the Investor promptly notifies the Company of such disclosure and takes reasonable steps to minimize the extent of any such required disclosure.

4. Rights to Future Stock Issuances.

4.1 Right of First Offer. Subject to the terms and conditions of this Section 4.1 and applicable securities laws, if the Company proposes to offer or sell any New Securities, the Company shall first offer such New Securities to each Major Investor. A Major Investor shall be entitled to apportion the right of first offer hereby granted to it among itself and its Affiliates in such proportions as it deems appropriate; provided that each such Affiliate agrees to enter into this Agreement and the Stockholders Agreement as an “Investor” under each such agreement.

(a) The Company shall give notice (the “**Offer Notice**”) to each Major Investor, stating (i) its bona fide intention to offer such New Securities, (ii) the number of such New Securities to be offered, and (iii) the price and terms, if any, upon which it proposes to offer such New Securities.

(b) By notification to the Company within twenty (20) days after the Offer Notice is given, each Major Investor may elect to purchase or otherwise acquire, at the price and on the terms specified in the Offer Notice, up to that portion of such New Securities which equals the proportion that the Common Stock then held by such Major Investor (including all shares of Common Stock then issuable (directly or indirectly) upon conversion and/or exercise, as applicable, of the Preferred Stock and any other Derivative Securities then held by such Major Investor) bears to the total number of shares of Common Stock of the Company then outstanding (assuming full conversion and/or exercise, as applicable, of all shares of Preferred Stock and other Derivative Securities). At the expiration of such twenty (20) day period, the Company shall promptly notify each Major Investor that elects to purchase or acquire all the shares available to it (each, a “**Fully Exercising Investor**”) of any other Major Investor’s failure to do likewise. During the ten (10) day period commencing after the Company has given such notice, each Fully Exercising Investor may, by giving notice to the Company, elect to purchase or acquire, in addition to the number of shares specified above, up to that portion of the New Securities for which Major Investors were entitled to subscribe but that were not subscribed for by the Major Investors, which portion is equal to the proportion that the Common Stock issued and held, or issuable upon conversion and/or exercise, as applicable, of Preferred Stock and any other Derivative Securities then held, by such Fully Exercising Investor bears to the number of shares of Common Stock issued and held, or issuable (directly or indirectly) upon conversion and/or exercise, as applicable, of the Preferred Stock and any other Derivative Securities then held, by all Fully Exercising Investors who wish to purchase such unsubscribed shares. The closing of any sale pursuant to this Section 4.1(b) shall occur within the later of one hundred twenty (120) days after the date that the Offer Notice is given and the date of initial sale of New Securities pursuant to Section 4.1(c).

(c) If all New Securities referred to in the Offer Notice are not elected to be purchased or acquired as provided in Section 4.1(b), the Company may, during the ninety (90) day period following the expiration of the periods provided in Section 4.1(b), offer and sell the remaining unsubscribed portion of such New Securities to any Person or Persons at a price not less than, and upon terms no more favorable to the offeree than, those specified in the Offer Notice. If the Company does not enter into an agreement for the sale of the New Securities within such period, or if such agreement is not consummated within thirty (30) days of the execution thereof, the right provided hereunder shall be deemed to be revived and such New

Securities shall not be offered unless first reoffered to the Major Investors in accordance with this Section 4.1.

(d) In the event that the rights of any Major Investor to purchase New Securities under this Section 4.1 are waived with respect to a particular offering of New Securities (the “Offering”) without such Major Investor’s prior written consent (a “Waived Investor”) and any Major Investor that participated in waiving such rights actually purchases New Securities in such offering, then the Company shall grant, and hereby grants, each Waived Investor the right to purchase, in a subsequent closing of such issuance on substantially the same terms and conditions and within 30 days of the initial closing of the Offering, the same percentage of its full pro rata share of such New Securities as the highest percentage of any such purchasing Major Investor.

(e) The right of first offer in this Section 4.1 shall not be applicable to (i) Exempted Securities (as defined in the Certificate of Incorporation), and (ii) shares of Common Stock issued in the IPO.

4.2 Termination. The covenants set forth in Section 4.1 shall terminate and be of no further force or effect upon the earliest to occur of (i) immediately before, but subject to, the consummation of the IPO, (ii) when the Company first becomes subject to the periodic reporting requirements of Section 12(g) or 15(d) of the Exchange Act, or (iii) upon a Deemed Liquidation Event.

5. Additional Covenants.

5.1 Insurance. Within a reasonable period of time after requested by the Board of Directors, the Company shall obtain from financially sound and reputable insurers Directors and Officers Errors and Omissions insurance in an amount satisfactory to the Board of Directors, and will use commercially reasonable efforts to cause such insurance policy to be maintained until such time as the Board of Directors determines that such insurance should be discontinued.

5.2 Employee Agreements. The Company will cause (i) each person now or hereafter employed by it or by any subsidiary (or engaged by the Company or any subsidiary as a consultant/independent contractor) with access to confidential information and/or trade secrets to enter into a nondisclosure and proprietary rights assignment agreement and (ii) each Key Employee to enter into a one (1) year noncompetition and nonsolicitation agreement, substantially in the form approved by the Board of Directors, including at least one Investor Director. In addition, the Company shall not amend, modify, terminate, waive, or otherwise alter, in whole or in part, any of the above-referenced agreements or any restricted stock agreement between the Company and any employee, without the approval by the Board of Directors, including at least one Investor Director.

5.3 Employee Vesting. Unless otherwise approved by the Board of Directors, which approval shall include at least one Investor Director, all current and future employees and consultants of the Company who purchase, receive options to purchase, or receive awards of shares of the Company’s capital stock after the date hereof shall be required to execute restricted

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stock or option agreements, as applicable, providing for (i) vesting of shares, not faster than, over a four (4) year period, with the first twenty-five percent (25%) of such shares vesting following twelve (12) months of continued employment or service, and the remaining shares vesting in equal monthly installments over the following three (3) years, and (ii) a market stand-off provision substantially similar to that in Section 2.11. In addition, unless otherwise approved by the Board of Directors, including at least one of the Investor Directors, the Company shall retain a “right of first refusal” on employee transfers until the Company’s IPO and shall have the right to repurchase unvested shares at cost upon termination of employment of a holder of restricted stock.

5.4 Matters Requiring Investor Director Approval. So long as any shares of Preferred Stock remain outstanding, the Company hereby covenants and agrees with each of the Investors that it shall not, without first obtaining the approval of the Board of Directors, which approval must include the affirmative vote of at least one Investor Director:

(a) make, or permit any subsidiary to make, any loan or advance to, or own any stock or other securities of, any subsidiary or other corporation, partnership, or other entity unless it is wholly owned by the Company;

(b) make, or permit any subsidiary to make, any loan or advance to any Person, including, without limitation, any employee or director of the Company or any subsidiary, except advances and similar expenditures in the ordinary course of business or under the terms of an employee stock or option plan approved by the Board of Directors;

(c) guarantee, directly or indirectly, or permit any subsidiary to guarantee, directly or indirectly, any indebtedness except for trade accounts of the Company or any subsidiary arising in the ordinary course of business;

(d) make any investment inconsistent with any investment policy approved by the Board of Directors;

(e) incur indebtedness in excess of \$75,000 in the aggregate that is not covered by the Budget, other than trade credit incurred in the ordinary course of business;

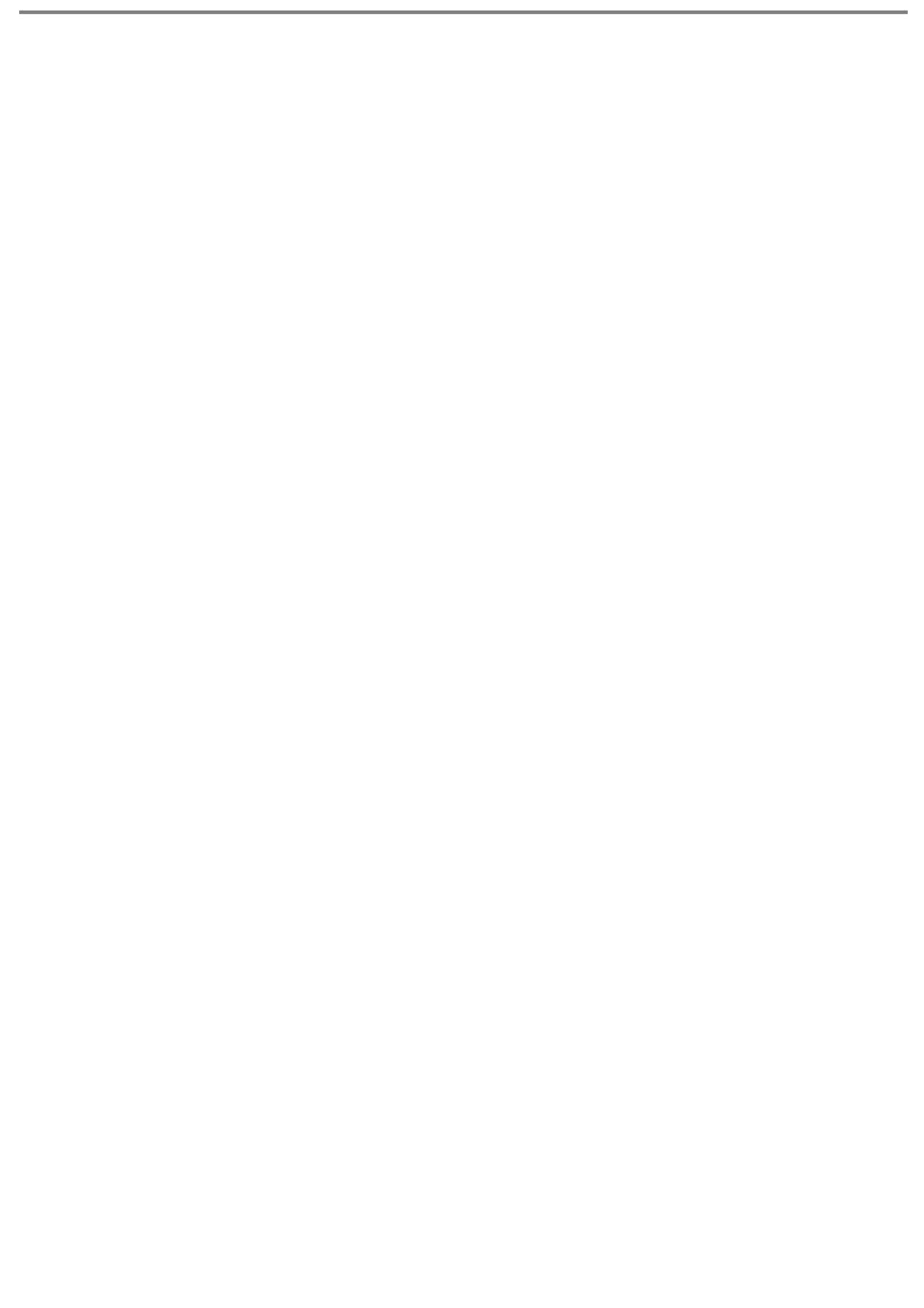
(f) otherwise enter into or be a party to any transaction with any director, officer or employee of the Company or any “associate” (as defined in Rule 12b-2 promulgated under the Exchange Act) of any such Person;

(g) hire, terminate, or change the compensation of the executive officers, including approving any option grants or stock awards to executive officers;

(h) change the principal business of the Company, or enter into a new line of business, or exit the existing line of business of the Company;

(i) sell, assign, license, pledge or encumber material technology or intellectual property, other than licenses granted in the ordinary course of business; or

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(j) enter into any corporate strategic relationship involving the payment contribution or assignment by the Company or to the Company of money or assets greater than \$200,000.

5.5 Meetings of the Board of Directors; Committees. Unless otherwise determined by the vote of a majority of the directors then in office, the Board of Directors shall meet at least four (4) times per year, and at least once per quarter, in accordance with an agreed-upon schedule, unless otherwise agreed by a vote of the majority of the directors. Each non-employee director shall be entitled in such person's discretion to be a member of any committee of the Board of Directors.

5.6 Successor Indemnification. If the Company or any of its successors or assignees consolidates with or merges into any other Person and is not the continuing or surviving corporation or entity of such consolidation or merger, then to the extent necessary, proper provision shall be made so that the successors and assignees of the Company assume the obligations of the Company with respect to indemnification of members of the Board of Directors as in effect immediately before such transaction, whether such obligations are contained in the Company's By-laws, the Certificate of Incorporation, or elsewhere, as the case may be.

5.7 Board Expenses. The Company shall reimburse the non-employee directors and board observers for all reasonable out-of-pocket expenses incurred (consistent with the Company's policies) in connection with their role as a director or a board observer of the Company.

5.8 Directors' Liability and Indemnification.

(a) The Certificate of Incorporation and By-laws (as such By-laws of the Company may be amended from time to time) shall provide (i) for limitation of the liability of directors to the maximum extent permitted by law, and (ii) for indemnification of directors for acts on behalf of the Company to the maximum extent permitted by law. In the event any suit is filed or claim is asserted against a director or former director of the Company as a result of such director's or former director's service on the Board of Directors, the Company will provide such director or former director access to all records and files of the Company as he or she may reasonably request in defending against or preparing to defend against any such suit or claim.

(b) The Company hereby acknowledges that one or more of the directors nominated by holders of Preferred Stock may have certain rights to indemnification, advancement of expenses and/or insurance provided by one or more of the Investors and certain of their affiliates (collectively, the "**Fund Indemnitors**") for alleged acts or omissions in their capacities as directors of the Company. The Company hereby agrees (i) that it is the indemnitor of first resort (i.e., its obligations to any such director are primary and any obligation of the Fund Indemnitors to advance expenses or to provide indemnification for the same expenses or liabilities incurred by such director are secondary), (ii) that it shall be required to advance the full amount of expenses incurred by such director and shall be liable for the full amount of all expenses, judgments, penalties, fines and amounts paid in settlement by or on behalf of any such director to the extent legally permitted and as required by the Certificate of Incorporation or By-

laws of the Company (or any agreement between the Company and such director), without regard to any rights such director may have against the Fund Indemnitors, and, (iii) that it irrevocably waives, relinquishes and releases the Fund Indemnitors from any and all claims against the Fund Indemnitors for contribution, subrogation or any other recovery of any kind in respect thereof. The Company further agrees that no advancement or payment by the Fund Indemnitors on behalf of any such director with respect to any claim for which such director has sought indemnification from the Company shall affect the foregoing and the Fund Indemnitors shall have a right of contribution and/or be subrogated to the extent of such advancement or payment to all of the rights of recovery of such director against the Company.

5.9 Right to Conduct Activities. The Company hereby agrees and acknowledges that certain of the Investors (together with their Affiliates) are professional investment organizations or funds or corporate venture capital entities, and as such invest in numerous portfolio companies, some of which may be deemed competitive with the Company's business (as currently conducted or as currently proposed to be conducted). The Company hereby agrees that, to the extent permitted under applicable law, such Investors shall not be liable to the Company for any claim arising out of, or based upon, (i) the investment by such Investors or their Affiliates in any entity competitive with the Company, or (ii) actions taken by any partner, officer or other representative of such Investor (or its Affiliates) to assist any such competitive company, whether or not such action was taken as a member of the board of directors of such competitive company or otherwise, and whether or not such action has a detrimental effect on the Company. Furthermore, the Company acknowledges that the execution of this Agreement and the access to the Company's confidential information hereunder shall in no way be construed to prohibit or restrict an Investor or its investment adviser or such investment adviser's other investment advisory clients from maintaining, making or considering investments in public or private companies, including, without limitation, companies that may compete either directly or indirectly with the Company, or from otherwise operating in the ordinary course of business. Notwithstanding anything in this Section 5.9 to the contrary, however, nothing herein shall relieve (x) any of the Investors from liability associated with the unauthorized disclosure of the Company's confidential information obtained pursuant to this Agreement, or (y) any director or officer of the Company from any liability associated with his or her fiduciary duties to the Company.

5.10 ERISA. The Company will exercise its reasonable best efforts to ensure that, at all times during which any Investor holds any shares of Preferred Stock or Common Stock, the assets of the Company will not be deemed to be "plan assets" for purposes of the Employee Retirement Income Security Act of 1974, as amended ("**ERISA**"). The Company agrees to provide notice, in writing, to each Investor as soon as is reasonably practicable upon determining that the assets of the Company are reasonably likely to be deemed "plan assets" for purposes of ERISA.

5.11 Termination of Covenants. The covenants set forth in this Section 5, except for Sections 5.6 and 5.8, shall terminate and be of no further force or effect upon the earliest to occur of (i) immediately before but subject to the consummation of an IPO; (ii) when the Company first becomes subject to the periodic reporting requirements of Section 12(g) or 15(d) of the Exchange Act; or (iii) upon a Deemed Liquidation Event.

6. Miscellaneous.

6.1 Successors and Assigns. The rights under this Agreement may be assigned (but only with all related obligations) by a Holder to a transferee of Registrable Securities that (i) is an Affiliate, partner, member, limited partner, retired partner, retired member, or stockholder of a Holder; (ii) is a Holder's Immediate Family Member or trust for the benefit of an individual Holder or one or more of such Holder's Immediate Family Members; or (iii) after such transfer, holds at least 1,000,000 shares of Registrable Securities (subject to appropriate adjustment for stock splits, stock dividends, combinations, and other recapitalizations), or, if less, all of the Registrable Securities held by such Holder; provided, however, that (x) the Company is, within a reasonable time after such transfer, furnished with written notice of the name and address of such transferee and the Registrable Securities with respect to which such rights are being transferred; and (y) such transferee agrees in a written instrument delivered to the Company to be bound by and subject to the terms and conditions of this Agreement, including the provisions of Section 2.11. For the purposes of determining the number of shares of Registrable Securities held by a transferee, the holdings of a transferee (1) that is an Affiliate, limited partner, retired partner, member, retired member, or stockholder of a Holder; (2) who is a Holder's Immediate Family Member; or (3) that is a trust for the benefit of an individual Holder or such Holder's Immediate Family Member shall be aggregated together and with those of the transferring Holder; provided further that all transferees who would not qualify individually for assignment of rights shall have a single attorney-in-fact for the purpose of exercising any rights, receiving notices, or taking any action under this Agreement. The terms and conditions of this Agreement inure to the benefit of and are binding upon the respective successors and permitted assignees of the parties, including without limitation, the Investor's affiliated partnership or funds management by such Investor or any of its respective directors, officers or partners. Nothing in this Agreement, express or implied, is intended to confer upon any party other than the parties hereto or their respective successors and permitted assignees any rights, remedies, obligations or liabilities under or by reason of this Agreement, except as expressly provided herein.

6.2 Governing Law. This Agreement shall be governed by and construed in accordance with the General Corporation Law of the State of Delaware as to matters within the scope thereof, and as to all other matters shall be governed by and construed in accordance with the internal laws of the Commonwealth of Massachusetts, without regard to conflict of law principles that would result in the application of any law other than the law of the Commonwealth of Massachusetts.

6.3 Counterparts; Facsimile. This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. This Agreement may also be executed and delivered by facsimile signature, email signature, or other form of electronic transmission.

6.4 Titles and Subtitles. The titles and subtitles used in this Agreement are for convenience only and are not to be considered in construing or interpreting this Agreement.

6.5 Notices. All notices, requests, and other communications given or made pursuant to this Agreement shall be in writing and shall be deemed effectively given, delivered

and received (i) upon personal delivery to the party to be notified; (ii) when sent by confirmed electronic mail or facsimile if sent during normal business hours of the recipient, and if not so confirmed, then on the next business day; (iii) five (5) days after having been sent by registered or certified mail, return receipt requested, postage prepaid; or (iv) one (1) business day after the business day of deposit with a nationally recognized overnight courier, specifying next-day delivery, with written verification of receipt. All communications shall be sent to the respective parties at their addresses as set forth on Schedule A hereto, or to the principal office of the Company and to the attention of the Chief Executive Officer, in the case of the Company, or to such email address, facsimile number, or address as subsequently modified by written notice given in accordance with this Section 6.5. If notice is given to the Company, a copy, which shall not constitute notice, shall also be sent to Lia Der Marderosian, Esq. at Wilmer Cutler Pickering Hale and Dorr LLP, 60 State Street, Boston, MA 02109 and via electronic mail at Lia.DerMarderosian@wilmerhale.com.

6.6 Amendments and Waivers. Any term of this Agreement, including without limitation Section 4.1, may be amended and the observance of any term of this Agreement may be waived (either generally or in a particular instance, and either retroactively or prospectively) only with the written consent of the Company and the holders representing the Requisite Vote; provided that the Company may in its sole discretion waive compliance with Section 2.12(c) (and the Company's failure to object promptly in writing after notification of a proposed assignment allegedly in violation of Section 2.12(c) shall be deemed to be a waiver); and provided further that any provision hereof may be waived by any waiving party on such party's own behalf, without the consent of any other party. Notwithstanding the foregoing, this Agreement may not be amended or terminated and the observance of any term hereof may not be waived with respect to any Investor without the written consent of such Investor, unless such amendment, termination, or waiver applies to all Investors in the same fashion (it being agreed that a waiver of the provisions of Section 4 with respect to a particular transaction shall be deemed to apply to all Investors in the same fashion if such waiver does so by its terms, notwithstanding the fact that certain Investors may nonetheless, by agreement with the Company, purchase securities in such transaction). The Company shall give prompt notice of any amendment or termination hereof or waiver hereunder to any party hereto that did not consent in writing to such amendment, termination, or waiver. Any amendment, termination, or waiver effected in accordance with this Section 6.6 shall be binding on all parties hereto, regardless of whether any such party has consented thereto. No waivers of or exceptions to any term, condition, or provision of this Agreement, in any one or more instances, shall be deemed to be or construed as a further or continuing waiver of any such term, condition, or provision.

6.7 Severability. In case any one or more of the provisions contained in this Agreement is for any reason held to be invalid, illegal or unenforceable in any respect, such invalidity, illegality, or unenforceability shall not affect any other provision of this Agreement, and such invalid, illegal, or unenforceable provision shall be reformed and construed so that it will be valid, legal, and enforceable to the maximum extent permitted by law.

6.8 Aggregation of Stock. All shares of Registrable Securities held or acquired by Affiliates shall be aggregated together for the purpose of determining the availability of any rights under this Agreement and such Affiliates may apportion such rights as among themselves in any manner they deem appropriate.

6.9 Additional Investors. Notwithstanding anything to the contrary contained herein, if the Company issues additional shares of the Series B Preferred Stock after the date hereof, any purchaser of such shares of Series B Preferred Stock may become a party to this Agreement by executing and delivering an additional counterpart signature page or joinder agreement to this Agreement, and thereafter shall be deemed an “Investor” for all purposes hereunder. No action or consent by the Investors shall be required for such joinder to this Agreement by such additional Investor, so long as such additional Investor has agreed in writing to be bound by all of the obligations as an “Investor” hereunder.

6.10 Entire Agreement. This Agreement (including any Schedules and Exhibits hereto) constitutes the full and entire understanding and agreement among the parties with respect to the subject matter hereof, and any other written or oral agreement relating to the subject matter hereof existing between the parties is expressly canceled. Upon the effectiveness of this Agreement, the Prior Agreement shall be deemed amended and restated and superseded and replaced in its entirety by this Agreement, and shall be of no further force or effect.

6.11 Delays or Omissions. No delay or omission to exercise any right, power, or remedy accruing to any party under this Agreement, upon any breach or default of any other party under this Agreement, shall impair any such right, power, or remedy of such nonbreaching or nondefaulting party, nor shall it be construed to be a waiver of or acquiescence to any such breach or default, or to any similar breach or default thereafter occurring, nor shall any waiver of any single breach or default be deemed a waiver of any other breach or default theretofore or thereafter occurring. All remedies, whether under this Agreement or by law or otherwise afforded to any party, shall be cumulative and not alternative.

6.12 Submission to Jurisdiction. The parties hereto submit to the exclusive jurisdiction of any federal or state court located within the Commonwealth of Massachusetts over any dispute arising out of or relating to the Agreement or any of the transactions contemplated hereby and each party hereby agree that all claims in respect of such dispute or any suit, action or proceeding related thereto may be heard and determined in such courts. The parties waive, to the fullest extent permitted by applicable law, any objection which they may not or hereafter have to the laying of venue of any such dispute brought in such court or any defense of inconvenient forum for the maintenance of such dispute. Each of the parties hereto agrees that a judgment in any such dispute may be enforced in other jurisdictions by suit on the judgment or in any other manner provided by law.

[Remainder of Page Intentionally Left Blank]

IN WITNESS WHEREOF, the parties have executed this Amended and Restated Investors' Rights Agreement as of the date first written above.

COMPANY:

FULCRUM THERAPEUTICS, INC.

By: /s/ Robert J. Gould
Name: Robert Gould
Title: Chief Executive Officer

[Signature Page to Amended and Restated Investors' Rights Agreement]

IN WITNESS WHEREOF, the parties have executed this Amended and Restated Investors' Rights Agreement as of the date first written above.

INVESTOR:

THIRD ROCK VENTURES III, L.P.

By: Third Rock Ventures GP III, L.P., its general partner
By: TRV GP III, LLC, its general partner

By: /s/ Kevin Gillis

Name: Kevin Gillis

Title: CFO

THIRD ROCK VENTURES IV, L.P.

By: Third Rock Ventures GP IV, L.P., its general partner
By: TRV GP IV, LLC, its general partner

By: /s/ Kevin Gillis

Name: Kevin Gillis

Title: CFO

[Signature Page to Amended and Restated Investors' Rights Agreement]

IN WITNESS WHEREOF, the parties have executed this Amended and Restated Investors' Rights Agreement as of the date first written above.

INVESTOR:

FORESITE CAPITAL FUND IV, L.P.

By: Foresite Capital Management IV, LLC,
its General Partner

By: /s/ Dennis D Ryan
Name: Dennis D. Ryan
Title: Chief Financial Officer

[Signature Page to Amended and Restated Investors' Rights Agreement]

IN WITNESS WHEREOF, the parties have executed this Amended and Restated Investors' Rights Agreement as of the date first written above.

**FIDELITY MT. VERNON STREET TRUST:
FIDELITY GROWTH COMPANY FUND**

By: /s/ Colm Hogan
Name: Colm Hogan
Title: Authorized Signatory

**FIDELITY MT. VERNON STREET TRUST:
FIDELITY SERIES GROWTH COMPANY FUND**

By: /s/ Colm Hogan
Name: Colm Hogan
Title: Authorized Signatory

FIDELITY GROWTH COMPANY COMMINGLED POOL

By: Fidelity Management Trust Company, as Trustee

By: /s/ Colm Hogan
Name: Colm Hogan
Title: Authorized Signatory

[Signature Page to Amended and Restated Investors' Rights Agreement]

IN WITNESS WHEREOF, the parties have executed this Amended and Restated Investors' Rights Agreement as of the date first written above.

CASDIN PARTNERS MASTER FUND, L.P.
By: Casdin Partners GP, LLC, its General Partner

By: /s/ Eli Casdin
Name: Eli Casdin
Title: Managing Member

[Signature Page to Amended and Restated Investors' Rights Agreement]

IN WITNESS WHEREOF, the parties have executed this Amended and Restated Investors' Rights Agreement as of the date first written above.

6 DIMENSIONS CAPITAL, L.P.

By: /s/ Christina Chung
Name: Christina Chung
Title: CFO

6 DIMENSIONS AFFILIATES FUND, L.P.

By: /s/ Christina Chung
Name: Christina Chung
Title: CFO

[Signature Page to Amended and Restated Investors' Rights Agreement]

IN WITNESS WHEREOF, the parties have executed this Amended and Restated Investors' Rights Agreement as of the date first written above.

SECTION 32 FUND 2, LP

By: Section 32 GP 2, LLC, its general partner

By: /s/ Jennifer L. Kercher

Name: Jennifer L. Kercher

Title: Chief Operating Officer

[Signature Page to Amended and Restated Investors' Rights Agreement]

IN WITNESS WHEREOF, the parties have executed this Amended and Restated Investors' Rights Agreement as of the date first written above.

INVESTOR:

AVENTIS INC.

By: /s/ Bernard Davitian

Name: Bernard Davitian

Title: SVP & Managing Director, Sanofi Ventures

[Signature Page to Amended and Restated Investors' Rights Agreement]

IN WITNESS WHEREOF, the parties have executed this Amended and Restated Investors' Rights Agreement as of the date first written above.

GBG-1 CORPORATION

By: /s/ Junkyu Park
Name: Junkyu Park
Title: Director

[Signature Page to Amended and Restated Investors' Rights Agreement]

IN WITNESS WHEREOF, the parties have executed this Amended and Restated Investors' Rights Agreement as of the date first written above.

MERITZ NS GLOBAL BIO FUND

Its co-managing partners

NS Investment Co., Ltd.

By: /s/ Tae-Kyoung Sohn

Name: Tae-Kyoung Sohn

Title: Managing director

Meritz Securities Co., Ltd.

By: /s/ Min-kyu Song

Name: Min-kyu Song

Title: Deputy General Manager

Paratus Investment Co., Ltd.

By: /s/ Chan-Ho Lee

Name: Chan-Ho Lee

Title: Managing Director

[Signature Page to Amended and Restated Investors' Rights Agreement]

IN WITNESS WHEREOF, the parties have executed this Amended and Restated Investors' Rights Agreement as of the date first written above.

LEERINK HOLDINGS LLC

By: /s/ Joseph R. Gentile
Name: Joseph R. Gentile
Title: CAO

LEERINK PARTNERS CO-INVESTMENT FUND, LLC

By: /s/ Joseph R. Gentile
Name: Joseph R. Gentile
Title: Manager

[Signature Page to Amended and Restated Investors' Rights Agreement]

PORTLAND INVESTMENT — EP, LLC

By: Partners Healthcare Master Trust for ERISA Assets, its Managing Member

By: /s/ John R. Barker
Name: John R. Barker
Title: Chief Investment Officer

PORTLAND INVESTMENT — PIA, LLC

By: Partners HealthCare System Pooled Investment Accounts, LLC, its Managing Member

By: /s/ John R. Barker
Name: John R. Barker
Title: Chief Investment Officer

PH INVESTMENTS, LLC

By: /s/ Benjamin A. Gomez
Name: Benjamin A. Gomez
Title: Managing Director

SCUBED CAPITAL, LLC

By: /s/ Mark Stevens
Name: Mark Stevens
Title: Managing Partner

FIFTH AVENUE PRIVATE EQUITY 14 LLC

By: /s/ Charles D. Bryceland
Name: Charles D. Bryceland
Title: Authorized Signatory

[Signature Page to Amended and Restated Investors' Rights Agreement]

IN WITNESS WHEREOF, the parties have executed this Amended and Restated Investors' Rights Agreement as of the date first written above.

SOBRATO CAPITAL,
a DBA of Sobrato Family Holdings, LLC,
a California limited liability company

By: /s/ Matthew W. Sonsini
Name: Matthew W. Sonsini
Title: Chief Executive Officer, on behalf of Sobrato Family Holdings, LLC

HARVARD MANAGEMENT PRIVATE EQUITY CORPORATION

By: /s/ Elise McDonald
Name: Elise McDonald
Title: Authorized Signatory

By: /s/ Richard W. Slocum
Name: Richard W. Slocum
Title: Authorized Signatory

[Signature Page to Amended and Restated Investors' Rights Agreement]

ADOPTION AGREEMENT

This Adoption Agreement ("**Adoption Agreement**") is executed on February 8, 2019, by the undersigned (the "**Holder**") pursuant to the terms of (i) that certain Amended and Restated Stockholders Agreement dated as of August 24, 2018 (as amended, restated, or otherwise modified from time to time, the "**Stockholders Agreement**"), by and among the Company and certain of its Stockholders, as such Agreement may be amended or amended and restated hereafter and (ii) that certain Amended and Restated Investors's Rights Agreement dated as of August 24, 2018 (as amended, restated, or otherwise modified from time to time, the "**IRA**"), by and among the Company and certain of its Stockholders, as such Agreement may be amended or amended and restated hereafter and Capitalized terms used but not defined in this Adoption Agreement shall have the respective meanings ascribed to such terms in the Stockholders Agreement and the IRA. By the execution of this Adoption Agreement, the Holder agrees as follows.

1.1 Acknowledgement. Holder acknowledges that Holder is acquiring certain shares of the capital stock of the Company (the "**Stock**") or options, warrants or other rights to purchase such Stock (the "**Options**"), for one of the following reasons (Check the correct box):

- as a transferee of Shares from a party in such party's capacity as an "Investor" bound by the Agreement, and after such transfer, Holder shall be considered an "Investor" and a "Stockholder" for all purposes of the Agreement.
- as a transferee of Shares from a party in such party's capacity as a "Key Holder" bound by the Agreement, and after such transfer, Holder shall be considered a "Key Holder" and a "Stockholder" for all purposes of the Agreement.
- as a new Investor in accordance with Section 8.2(a) of the Stockholders Agreement, in which case Holder will be an "Investor" and a "Stockholder" for all purposes of the Stockholders Agreement and in accordance with Section 6.9 of the IRA, in which case Holder will be an "Investor" and a "Holder" for all purposes under the IRA, and shall be deemed a "Major Investor" for all purposes under the IRA so long as Holder, individually or together with such Holder's Affiliates (as defined in the IRA), holds at least 750,000 shares of Registrable Securities (as defined in the IRA) in accordance with Section 1.21 of the IRA.
- in accordance with Section 8.2(b) of the Agreement, as a new party who is not a new Investor, in which case Holder will be a "Key Holder" and a "Stockholder" for all purposes of the Agreement.

1.2 Agreement. Holder hereby (a) agrees that the Stock and any other shares of capital stock or securities required by the Stockholders Agreement and the IRA to be bound thereby, shall be bound by and subject to the terms of the Stockholders Agreement and IRA, respectively and (b) adopts the Stockholders Agreement and the IRA with the same force and effect as if Holder were originally a party to each such agreement.

1.3 Notice. Any notice required or permitted by Stockholders Agreement and the IRA shall be given to Holder at the address or facsimile number listed below Holder's signature hereto.

(Signature Page Follows)

GLAXO GROUP LIMITED

ACCEPTED AND AGREED:

By: /s/ John Sadler

FULCRUM THERAPEUTICS, INC.

Name: John Sadler
Title: Authorised Signatory
For and on behalf of
Edinburgh Pharmaceutical
Industries Limited
Corporate Director

Address:
980 Great West Road
Brentford, Middlesex
TW8 9GS England

By: /s/ Robert J. Gould

Title: President & CEO

SCHEDULE A

Name and Contact of Investors

THIRD ROCK VENTURES III, L.P.

29 Newbury Street; 3rd Floor
Boston, MA 02116

GV 2016, L.P.

Attn: Daphne Chang
c/o GV
1600 Amphitheatre Parkway
Mountain View, CA 94043

THIRD ROCK VENTURES IV, L.P.

29 Newbury Street; 3rd Floor
Boston, MA 02116

FORESITE CAPITAL FUND IV, L.P.

600 Montgomery Street, Suite 4500
San Francisco, CA 94111

AVENTIS INC.

55 Corporate Drive
Bridgewater, New Jersey 08807
Attn: General Counsel, NA

With a copy which should not constitute notice to:
Sanofi Ventures
50 Binney Street — 02142 CAMBRIDGE — USA
Attn: Jason Hafler

SECTION 32 FUND 2, LP

2033 San Elijo Avenue, #565
Cardiff by the Sea, CA 92007

PH INVESTMENTS, LLC

Pilot House, Lewis Wharf
Boston, MA 02110
Attention: Ben Gomez; John Vander Vort;
April Robinson

SCUBED CAPITAL, LLC

2061 Avy Avenue
Menlo Park, CA 94025
Attn: Mark Stevens; Margo Doyle

SOBRATO CAPITAL

Sobrato Family Holdings, LLC
10600 N. De Anza Blvd., Suite 200
Cupertino, CA 95014
Attn: Matt Sonsini and Albert Chiang

HARVARD MANAGEMENT PRIVATE EQUITY CORPORATION

600 Atlantic Avenue
Boston, MA 02210
Attn: Elise McDonald and Emily Carroll

PORTLAND INVESTMENT — EP, LLC

Partners HealthCare Investment Office
101 Merrimac St., 8th Floor
Boston, MA 02114
Attn: Kate Kamm, Portfolio Manager

PORTLAND INVESTMENT — PIA, LLC

Partners HealthCare Investment Office
101 Merrimac St., 8th Floor
Boston, MA 02114
Attn: Kate Kamm, Portfolio Manager

FIFTH AVENUE PRIVATE EQUITY 14 LLC

630 Fifth Avenue
New York, NY 10111

LEERINK HOLDINGS LLC

One Federal Street,
37th Floor,
Boston, MA 02110
Attention: General Counsel

LEERINK PARTNERS CO-INVESTMENT FUND, LLC

One Federal Street,
37th Floor,
Boston, MA 02110
Attention: General Counsel

CASDIN PARTNERS MASTER FUND, L.P.

1350 Avenue of the Americas, Suite 2405
New York, New York 10019

FIDELITY MT. VERNON STREET TRUST: FIDELITY GROWTH COMPANY FUND

BNY Mellon
Attn: Stacey Wolfe
525 William Penn Place Rm 0400
Pittsburgh, PA 15259

FIDELITY MT. VERNON STREET TRUST: FIDELITY SERIES GROWTH COMPANY FUND

State Street Bank & Trust
PO Box 5756
Boston, Massachusetts 02206
Attn: WAVELENGTH + CO Fidelity Mt. Vernon Street Trust: Fidelity Series Growth Company Fund

FIDELITY GROWTH COMPANY COMMINGLED POOL

Mag & Co.
c/o Brown Brothers Harriman & Co.
Attn: Corporate Actions /Vault
140 Broadway
New York, NY 10005

6 DIMENSIONS CAPITAL, L.P.

P.O. Box 309, Ugland House Grand Cayman,
KY1-1104, Cayman Islands

6 DIMENSIONS AFFILIATES FUND, L.P.

P.O. Box 309, Ugland House Grand Cayman,
KY1-1104, Cayman Islands

GBG-1 CORPORATION

Walkers Corporate Limited, Cayman Corporate Center
27 Hospital Road
George Town, Grand Cayman KY1-9008
Cayman Islands

MERITZ NS GLOBAL BIO FUND

15, Gukjegeumyung-ro 6-gil
Yeongdeungpo-gu, Seoul
Republic of Korea 07330

GLAXO GROUP LIMITED

980 Great West Road
Brentford, Middlesex
TW8 9GS England

2016 STOCK INCENTIVE PLAN
OF
FULCRUM THERAPEUTICS, INC.

(Adopted by the Board of Directors and approved by the stockholders on July 11, 2016)

(First amendment adopted by the Board of Directors on August 2, 2017)

(First amendment approved by the stockholders on August 9, 2017)

(Second amendment adopted by the Board of Directors on January 23, 2018)

(Second amendment approved by the stockholders on January 23, 2018)

(Third amendment adopted by the Board of Directors on August 23, 2018)

(Third amendment approved by the stockholders on August 23, 2018)

(Fourth amendment adopted by the Board of Directors on February 6, 2019)

(Fourth amendment approved by the stockholders on February 7, 2019)

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2016 STOCK INCENTIVE PLAN

OF

Fulcrum Therapeutics, Inc.

1. Purpose

The purpose of this 2016 Stock Incentive Plan (the “**Plan**”) of Fulcrum Therapeutics, Inc., a Delaware corporation (the “**Company**”), is to advance the interests of the Company’s stockholders by enhancing the Company’s ability to attract, retain and motivate persons who are expected to make important contributions to the Company and by providing such persons with equity ownership opportunities and performance-based incentives that are intended to better align the interests of such persons with those of the Company’s stockholders. Except where the context otherwise requires, the term “**Company**” shall include any of the Company’s present or future parent or subsidiary corporations as defined in Sections 424(e) or (f) of the Internal Revenue Code of 1986, as amended, and any regulations thereunder (the “**Code**”) and any other business venture (including, without limitation, joint venture or limited liability company) in which the Company has a controlling interest, as determined by the Board of Directors of the Company (the “**Board**”); *provided, however*, that such other business ventures shall be limited to entities that, where required by Section 409A of the Code, are eligible issuers of service recipient stock (as defined in Treas. Reg. Section 1.409A-1(b)(5)(iii)(E), or applicable successor regulation).

2. Eligibility

All of the Company’s employees, officers and directors, as well as consultants and advisors to the Company (as such terms consultants and advisors are defined and interpreted for purposes of Rule 701 under the Securities Act of 1933, as amended (the “**Securities Act**”) (or any successor rule)) are eligible to be granted Awards under the Plan. Each person who is granted an Award under the Plan is deemed a “**Participant**.” “**Award**” means Options (as defined in Section 5), SARs (as defined in Section 6), Restricted Stock (as defined in Section 7), Restricted Stock Units (as defined in Section 7) and Other Stock-Based Awards (as defined in Section 8).

3. Administration and Delegation

(a) Administration by the Board. The Plan will be administered by the Board. The Board shall have authority to grant Awards and to adopt, amend and repeal such administrative rules, guidelines and practices relating to the Plan as it shall deem advisable. The Board may construe and interpret the terms of the Plan and any Award agreements entered into under the Plan. The Board may correct any defect, supply any omission or reconcile any inconsistency in the Plan or any Award in the manner and to the extent it shall deem expedient to carry the Plan into effect and it shall be the sole and final judge of such expediency. All decisions by the Board shall be made in the Board’s sole discretion and shall be final and binding on all persons having or claiming any interest in the Plan or in any Award.

(b) Appointment of Committees. To the extent permitted by applicable law, the Board may delegate any or all of its powers under the Plan to one or more committees or subcommittees of the Board (each, a “**Committee**”). All references in the Plan to the “**Board**” shall mean the Board or a Committee of the Board to the extent that the Board’s powers or authority under the Plan have been delegated to such Committee.

4. Stock Available for Awards

(a) Number of Shares. Subject to adjustment under Section 9, Awards may be made under the Plan for up to 24,965,000 shares of common stock, \$0.001 par value per share, of the Company (the “**Common Stock**”), any or all of which Awards may be in the form of Incentive Stock Options (as defined in Section 5(b)). If any Award expires or is terminated, surrendered or canceled without having been fully exercised, is forfeited in whole or in part (including as the result of shares of Common Stock subject to such Award being repurchased by the Company at the original issuance price pursuant to a contractual repurchase right), or results in any Common Stock not being issued, the unused Common Stock covered by such Award shall again be available for the grant of Awards under the Plan. Further, shares of Common Stock tendered to the Company by a Participant to exercise an Award or to satisfy tax withholding obligations arising with respect to an Award shall be added to the number of shares of Common Stock available for the grant of Awards under the Plan. However, in the case of Incentive Stock Options, the two immediately preceding sentences shall be subject to any limitations under the Code. Shares issued under the Plan may consist in whole or in part of authorized but unissued shares or treasury shares.

(b) Substitute Awards. In connection with a merger or consolidation of an entity with the Company or the acquisition by the Company of property or stock of an entity, the Board may grant Awards in substitution for any options or other stock or stock-based awards granted by such entity or an affiliate thereof. Substitute Awards may be granted on such terms as the Board deems appropriate in the circumstances, notwithstanding any limitations on Awards contained in the Plan. Substitute Awards shall not count against the overall share limit set forth in Section 4(a), except as may be required by reason of Section 422 and related provisions of the Code.

5. Stock Options

(a) General. The Board may grant options to purchase Common Stock (each, an “**Option**”) and determine the number of shares of Common Stock to be covered by each Option, the exercise price of each Option and the conditions and limitations applicable to the exercise of each Option, including conditions relating to applicable federal or state securities laws, as it considers necessary or advisable.

(b) Incentive Stock Options. An Option that the Board intends to be an “incentive stock option” as defined in Section 422 of the Code (an “**Incentive Stock Option**”) shall only be granted to employees of Fulcrum Therapeutics, Inc., any of Fulcrum Therapeutics, Inc.’s present or future parent or subsidiary corporations as defined in Sections 424(e) or (f) of the Code, and any other entities the employees of which are eligible to receive Incentive Stock Options under the Code, and shall be subject to and shall be construed consistently with the requirements of Section 422 of the Code. An Option that is not intended to be an Incentive Stock Option shall be

designated a “**Nonstatutory Stock Option**.” The Company shall have no liability to a Participant, or any other party, if an Option (or any part thereof) that is intended to be an Incentive Stock Option is not an Incentive Stock Option or if the Company converts an Incentive Stock Option to a Nonstatutory Stock Option.

(c) Exercise Price. The Board shall establish the exercise price of each Option and specify the exercise price in the applicable Option agreement. The exercise price shall be not less than 100% of the fair market value per share of Common Stock, as determined by (or in a manner approved by) the Board (“**Fair Market Value**”), on the date the Option is granted. “**Fair Market Value**” of a share of Common Stock for purposes of the Plan will be determined as follows:

(1) if the Common Stock is not publicly traded, the Board will determine the Fair Market Value for purposes of the Plan using any measure of value it determines to be appropriate (including, as it considers appropriate, relying on appraisals) in a manner consistent with the valuation principles under Code Section 409A, except as the Board may expressly determine otherwise;

(2) if the Common Stock trades on a national securities exchange, the closing sale price (for the primary trading session) on the date of grant; or

(3) if the Common Stock does not trade on any such exchange, the average of the closing bid and asked prices as reported by an authorized OTCBB market data vendor as listed on the OTCBB website (otcbb.com) on the date of grant.

For any date that is not a trading day, the Fair Market Value of a share of Common Stock for such date will be determined by using the closing sale price or average of the bid and asked prices, as appropriate, for the immediately preceding trading day and with the timing in the formulas above adjusted accordingly. The Board can substitute a particular time of day or other measure of “closing sale price” or “bid and asked prices” if appropriate because of exchange or market procedures or can, in its sole discretion, use weighted averages either on a daily basis or such longer period as complies with Code Section 409A.

The Board has sole discretion to determine the Fair Market Value for purposes of the Plan, and all Awards are conditioned on the participants’ agreement that the Board’s determination is conclusive and binding even though others might make a different determination.

(d) Duration of Options. Each Option shall be exercisable at such times and subject to such terms and conditions as the Board may specify in the applicable option agreement; *provided, however*, that no Option will be granted with a term in excess of 10 years.

(e) Exercise of Options.

(1) Options may be exercised by delivery to the Company of a notice of exercise in a form of notice (which may be electronic) approved by the Company, together with payment in full (in a manner specified in Section 5(f)) of the exercise price for the number of

shares for which the Option is exercised. Shares of Common Stock subject to the Option will be delivered by the Company as soon as practicable following exercise.

(f) Payment Upon Exercise. Common Stock purchased upon the exercise of an Option granted under the Plan shall be paid for as follows:

(1) in cash or by check, payable to the order of the Company;

(2) when the Common Stock is registered under the Securities Exchange Act of 1934, as amended (the “**Exchange Act**”), except as may otherwise be provided in the applicable Option agreement or approved by the Board, in its sole discretion, by (i) delivery of an irrevocable and unconditional undertaking by a creditworthy broker to deliver promptly to the Company sufficient funds to pay the exercise price and any required tax withholding or (ii) delivery by the Participant to the Company of a copy of irrevocable and unconditional instructions to a creditworthy broker to deliver promptly to the Company cash or a check sufficient to pay the exercise price and any required tax withholding;

(3) when the Common Stock is registered under the Exchange Act and to the extent provided for in the applicable Option agreement or approved by the Board, in its sole discretion, by delivery (either by actual delivery or attestation) of shares of Common Stock owned by the Participant valued at their Fair Market Value, *provided* (i) such method of payment is then permitted under applicable law, (ii) such Common Stock, if acquired directly from the Company, was owned by the Participant for such minimum period of time, if any, as may be established by the Board in its discretion and (iii) such Common Stock is not subject to any repurchase, forfeiture, unfulfilled vesting or other similar requirements;

(4) to the extent provided for in the applicable Nonstatutory Stock Option agreement or approved by the Board in its sole discretion, by delivery of a notice of “net exercise” to the Company, as a result of which the Participant would pay the exercise price for the portion of the Option being exercised by cancelling a portion of the Option for such number of shares as is equal to the exercise price divided by the excess of the Fair Market Value on the date of exercise over the Option exercise price per share.

(5) to the extent permitted by applicable law and provided for in the applicable Option agreement or approved by the Board, in its sole discretion, by (i) delivery of a promissory note of the Participant to the Company on terms determined by the Board, or (ii) payment of such other lawful consideration as the Board may determine; or

(6) by any combination of the above permitted forms of payment.

6. Stock Appreciation Rights

(a) General. The Board may grant Awards consisting of stock appreciation rights (“SARs”) entitling the holder, upon exercise, to receive an amount of Common Stock or cash or a combination thereof (such form to be determined by the Board) determined by reference to appreciation, from and after the date of grant, in the Fair Market Value of a share of Common Stock over the measurement price established pursuant to Section 6(b). The date as of which such appreciation is determined shall be the exercise date.

(b) Measurement Price. The Board shall establish the measurement price of each SAR and specify it in the applicable SAR agreement. The measurement price shall not be less than 100% of the Fair Market Value on the date the SAR is granted.

(c) Duration of SARs. Each SAR shall be exercisable at such times and subject to such terms and conditions as the Board may specify in the applicable SAR agreement; *provided, however*, that no SAR will be granted with a term in excess of 10 years.

(d) Exercise of SARs. SARs may be exercised by delivery to the Company of a notice of exercise in a form (which may be electronic) approved by the Company, together with any other documents required by the Board.

7. Restricted Stock; Restricted Stock Units

(a) General. The Board may grant Awards entitling recipients to acquire shares of Common Stock (“**Restricted Stock**”), subject to the right of the Company to repurchase all or part of such shares at their issue price or other stated or formula price (or to require forfeiture of such shares if issued at no cost) from the recipient in the event that conditions specified by the Board in the applicable Award are not satisfied prior to the end of the applicable restriction period or periods established by the Board for such Award. The Board may also grant Awards entitling the recipient to receive shares of Common Stock or cash to be delivered at the time such Award vests (“**Restricted Stock Units**”) (Restricted Stock and Restricted Stock Units are each referred to herein as a “**Restricted Stock Award**”).

(b) Terms and Conditions for All Restricted Stock Awards. The Board shall determine the terms and conditions of a Restricted Stock Award, including the conditions for vesting and repurchase (or forfeiture) and the issue price, if any.

(c) Additional Provisions Relating to Restricted Stock.

(1) Dividends. Unless otherwise provided in the applicable Award agreement, any dividends (whether paid in cash, stock or property) declared and paid by the Company with respect to shares of Restricted Stock (“**Accrued Dividends**”) shall be paid to the Participant only if and when such shares become free from the restrictions on transferability and forfeitability that apply to such shares. Each payment of Accrued Dividends will be made no later than the end of the calendar year in which the dividends are paid to stockholders of that class of stock or, if later, the 15th day of the third month following the lapsing of the restrictions on transferability and the forfeitability provisions applicable to the underlying shares of Restricted Stock.

(2) Stock Certificates. The Company may require that any stock certificates issued in respect of shares of Restricted Stock, as well as dividends or distributions paid on such Restricted Stock, shall be deposited in escrow by the Participant, together with a stock power endorsed in blank, with the Company (or its designee). At the expiration of the applicable restriction periods, the Company (or such designee) shall deliver the certificates no longer subject to such restrictions to the Participant or if the Participant has died, to Participant's Designated Beneficiary. "**Designated Beneficiary**" means (i) the beneficiary designated, in a manner determined by the Board, by a Participant to receive amounts due or exercise rights of the Participant in the event of the Participant's death or (ii) in the absence of an effective designation by a Participant, "**Designated Beneficiary**" means the Participant's estate.

(d) Additional Provisions Relating to Restricted Stock Units.

(1) Settlement. Upon the vesting of and/or lapsing of any other restrictions (i.e., settlement) with respect to each Restricted Stock Unit, the Participant shall be entitled to receive from the Company one share of Common Stock or (if so provided in the applicable Award agreement) an amount of cash equal to the Fair Market Value of one share of Common Stock. The Board may, in its discretion, provide that settlement of Restricted Stock Units shall be deferred, on a mandatory basis or at the election of the Participant in a manner that complies with Section 409A of the Code.

(2) Voting Rights. A Participant shall have no voting rights with respect to any Restricted Stock Units.

(3) Dividend Equivalents. The Award agreement for Restricted Stock Units may provide Participants with the right to receive an amount equal to any dividends or other distributions declared and paid on an equal number of outstanding shares of Common Stock ("**Dividend Equivalents**"). Dividend Equivalents may be paid currently or credited to an account for the Participants, may be settled in cash and/or shares of Common Stock and may be subject to the same restrictions on transfer and forfeitability as the Restricted Stock Units with respect to which paid, in each case to the extent provided in the applicable Award agreement.

8. Other Stock-Based Awards

(a) General. Other Awards of shares of Common Stock, and other Awards that are valued in whole or in part by reference to, or are otherwise based on, shares of Common Stock or other property, may be granted hereunder to Participants ("**Other Stock-Based Awards**"). Such Other Stock-Based Awards shall also be available as a form of payment in the settlement of other Awards granted under the Plan or as payment in lieu of compensation to which a Participant is otherwise entitled. Other Stock-Based Awards may be paid in shares of Common Stock or cash, as the Board shall determine.

(b) Terms and Conditions. Subject to the provisions of the Plan, the Board shall determine the terms and conditions of each Other Stock-Based Award, including any purchase price applicable thereto.

9. Adjustments for Changes in Common Stock and Certain Other Events

(a) Changes in Capitalization. In the event of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, spin-off or other similar change in capitalization or event, or any dividend or distribution to holders of Common Stock other than an ordinary cash dividend, (i) the number and class of securities available under the Plan, (ii) the number and class of securities and exercise price per share of each outstanding Option, (iii) the share and per-share provisions and the measurement price of each outstanding SAR, (iv) the number of shares subject to and the repurchase price per share subject to each outstanding Restricted Stock Award and (v) the share and per-share-related provisions and the purchase price, if any, of each outstanding Other Stock-Based Award, shall be equitably adjusted by the Company (or substituted Awards may be made, if applicable) in the manner determined by the Board. Without limiting the generality of the foregoing, in the event the Company effects a split of the Common Stock by means of a stock dividend and the exercise price of and the number of shares subject to an outstanding Option are adjusted as of the date of the distribution of the dividend (rather than as of the record date for such dividend), then an optionee who exercises an Option between the record date and the distribution date for such stock dividend shall be entitled to receive, on the distribution date, the stock dividend with respect to the shares of Common Stock acquired upon such Option exercise, notwithstanding the fact that such shares were not outstanding as of the close of business on the record date for such stock dividend.

(b) Reorganization Events.

(1) Definition. A “**Reorganization Event**” shall mean: (a) any merger or consolidation of the Company with or into another entity as a result of which all of the Common Stock of the Company is converted into or exchanged for the right to receive cash, securities or other property or is cancelled, (b) any transfer or disposition of all of the Common Stock of the Company for cash, securities or other property pursuant to a share exchange or other transaction or (c) any liquidation or dissolution of the Company.

(2) Consequences of a Reorganization Event on Awards Other than Restricted Stock.

(i) In connection with a Reorganization Event, the Board may take any one or more of the following actions as to all or any (or any portion of) outstanding Awards other than Restricted Stock on such terms as the Board determines (except to the extent specifically provided otherwise in an applicable Award agreement or another agreement between the Company and the Participant): (i) provide that such Awards shall be assumed, or substantially equivalent Awards shall be substituted, by the acquiring or succeeding corporation (or an affiliate thereof), (ii) upon written notice to a Participant, provide that all of the Participant’s unexercised Awards will terminate immediately prior to the consummation of such Reorganization Event unless exercised by the Participant (to the extent then exercisable) within a specified period following the date of such notice, (iii) provide that outstanding Awards shall become exercisable, realizable, or deliverable, or restrictions applicable to an Award shall lapse, in whole or in part prior to or upon such Reorganization Event, (iv) in the event of a Reorganization Event under the terms of which holders of Common Stock will receive upon

consummation thereof a cash payment for each share surrendered in the Reorganization Event (the “**Acquisition Price**”), make or provide for a cash payment to Participants with respect to each Award held by a Participant equal to (A) the number of shares of Common Stock subject to the vested portion of the Award (after giving effect to any acceleration of vesting that occurs upon or immediately prior to such Reorganization Event) multiplied by (B) the excess, if any, of (I) the Acquisition Price over (II) the exercise, measurement or purchase price of such Award and any applicable tax withholdings, in exchange for the termination of such Award, (v) provide that, in connection with a liquidation or dissolution of the Company, Awards shall convert into the right to receive liquidation proceeds (if applicable, net of the exercise, measurement or purchase price thereof and any applicable tax withholdings) and (vi) any combination of the foregoing. In taking any of the actions permitted under this Section 9(b)(2), the Board shall not be obligated by the Plan to treat all Awards, all Awards held by a Participant, or all Awards of the same type, identically.

(ii) Notwithstanding the terms of Section 9(b)(2)(i), in the case of outstanding Restricted Stock Units that are subject to Section 409A of the Code: (i) if the applicable Restricted Stock Unit agreement provides that the Restricted Stock Units shall be settled upon a “change in control event” within the meaning of Treasury Regulation Section 1.409A-3(i)(5)(i), and the Reorganization Event constitutes such a “change in control event”, then no assumption or substitution shall be permitted pursuant to Section 9(b)(2)(i)(i) and the Restricted Stock Units shall instead be settled in accordance with the terms of the applicable Restricted Stock Unit agreement; and (ii) the Board may only undertake the actions set forth in clauses (iii), (iv) or (v) of Section 9(b)(2)(i) if the Reorganization Event constitutes a “change in control event” as defined under Treasury Regulation Section 1.409A-3(i)(5)(i) and such action is permitted or required by Section 409A of the Code; if the Reorganization Event is not a “change in control event” as so defined or such action is not permitted or required by Section 409A of the Code, and the acquiring or succeeding corporation does not assume or substitute the Restricted Stock Units pursuant to clause (i) of Section 9(b)(2)(i), then the unvested Restricted Stock Units shall terminate immediately prior to the consummation of the Reorganization Event without any payment in exchange therefor.

(iii) For purposes of Section 9(b)(2)(i)(i), an Award (other than Restricted Stock) shall be considered assumed if, following consummation of the Reorganization Event, such Award confers the right to purchase or receive pursuant to the terms of such Award, for each share of Common Stock subject to the Award immediately prior to the consummation of the Reorganization Event, the consideration (whether cash, securities or other property) received as a result of the Reorganization Event by holders of Common Stock for each share of Common Stock held immediately prior to the consummation of the Reorganization Event (and if holders were offered a choice of consideration, the type of consideration chosen by the holders of a majority of the outstanding shares of Common Stock); *provided, however*, that if the consideration received as a result of the Reorganization Event is not solely common stock of the acquiring or succeeding corporation (or an affiliate thereof), the Company may, with the consent of the acquiring or succeeding corporation, provide for the consideration to be received upon the exercise or settlement of the Award to consist solely of such number of shares of common stock of the acquiring or succeeding corporation (or an affiliate thereof) that the Board determined to be equivalent in value (as of the date of such determination or another date specified by the

Board) to the per share consideration received by holders of outstanding shares of Common Stock as a result of the Reorganization Event.

(3) Consequences of a Reorganization Event on Restricted Stock. Upon the occurrence of a Reorganization Event other than a liquidation or dissolution of the Company, the repurchase and other rights of the Company with respect to outstanding Restricted Stock shall inure to the benefit of the Company's successor and shall, unless the Board determines otherwise, apply to the cash, securities or other property which the Common Stock was converted into or exchanged for pursuant to such Reorganization Event in the same manner and to the same extent as they applied to such Restricted Stock; *provided, however*, that the Board may provide for termination or deemed satisfaction of such repurchase or other rights under the instrument evidencing any Restricted Stock or any other agreement between a Participant and the Company, either initially or by amendment. Upon the occurrence of a Reorganization Event involving the liquidation or dissolution of the Company, except to the extent specifically provided to the contrary in the instrument evidencing any Restricted Stock or any other agreement between a Participant and the Company, all restrictions and conditions on all Restricted Stock then outstanding shall automatically be deemed terminated or satisfied.

10. General Provisions Applicable to Awards.

(a) Transferability of Awards. Awards (or any interest in an Award, including, prior to exercise, any interest in shares of Common Stock issuable upon exercise of an Option or SAR) shall not be sold, assigned, transferred (including by establishing any short position, put equivalent position (as defined in Rule 16a-1 issued under the Exchange Act) or call equivalent position (as defined in Rule 16a-1 issued under the Exchange Act)), pledged, hypothecated or otherwise encumbered by the person to whom they are granted, either voluntarily or by operation of law, and, during the life of the Participant, shall be exercisable only by the Participant; except that Awards, other than Awards subject to Section 409A of the Code, may be transferred to family members (as defined in Rule 701(c)(3) under the Securities Act) through gifts or (other than Incentive Stock Options) domestic relations orders or to an executor or guardian upon the death of the Participant. The Company shall not be required to recognize any such permitted transfer until such time as such permitted transferee shall deliver to the Company a written instrument, as a condition to such transfer, in form and substance satisfactory to the Company confirming that such transferee shall be bound by all of the terms and conditions of the Award. References to a Participant, to the extent relevant in the context, shall include references to authorized transferees. For the avoidance of doubt, nothing contained in this Section 10(a) shall be deemed to restrict a transfer to the Company.

(b) Documentation. Each Award shall be evidenced in such form (written, electronic or otherwise) as the Board shall determine. Each Award may contain terms and conditions in addition to those set forth in the Plan.

(c) Board Discretion. Except as otherwise provided by the Plan, each Award may be made alone or in addition or in relation to any other Award. The terms of each Award need not be identical, and the Board need not treat Participants uniformly.

(d) Termination of Status. The Board shall determine the effect on an Award of the disability, death, termination or other cessation of employment, authorized leave of absence or other change in the employment or other status of a Participant and the extent to which, and the period during which, the Participant, or the Participant's legal representative, conservator, guardian or Designated Beneficiary, may exercise rights under the Award.

(e) Withholding. The Participant must satisfy all applicable federal, state, and local or other income and employment tax withholding obligations before the Company will deliver stock certificates or otherwise recognize ownership of Common Stock under an Award. The Company may decide to satisfy the withholding obligations through additional withholding on salary or wages. If the Company elects not to or cannot withhold from other compensation, the Participant must pay the Company the full amount, if any, required for withholding or have a broker tender to the Company cash equal to the withholding obligations. Payment of withholding obligations is due before the Company will issue any shares on exercise, vesting or release from forfeiture of an Award or at the same time as payment of the exercise or purchase price unless the Company determines otherwise. If provided for in an Award or approved by the Board in its sole discretion, a Participant may satisfy such tax obligations in whole or in part by delivery (either by actual delivery or attestation) of shares of Common Stock, including shares retained from the Award creating the tax obligation, valued at their Fair Market Value; *provided, however*, except as otherwise provided by the Board, that the total tax withholding where stock is being used to satisfy such tax obligations cannot exceed the Company's minimum statutory withholding obligations (based on minimum statutory withholding rates for federal and state tax purposes, including payroll taxes, that are applicable to such supplemental taxable income). Shares used to satisfy tax withholding requirements cannot be subject to any repurchase, forfeiture, unfulfilled vesting or other similar requirements.

(f) Amendment of Award.

(1) The Board may amend, modify or terminate any outstanding Award, including but not limited to, substituting therefor another Award of the same or a different type, changing the date of exercise or realization, and converting an Incentive Stock Option to a Nonstatutory Stock Option. The Participant's consent to such action shall be required unless (i) the Board determines that the action, taking into account any related action, does not materially and adversely affect the Participant's rights under the Plan or (ii) the change is permitted under Section 9.

(2) The Board may, without stockholder approval, amend any outstanding Award granted under the Plan to provide an exercise price per share that is lower than the then-current exercise price per share of such outstanding Award. The Board may also, without stockholder approval, cancel any outstanding award (whether or not granted under the Plan) and grant in substitution therefor new Awards under the Plan covering the same or a different number of shares of Common Stock and having an exercise price per share lower than the then-current exercise price per share of the cancelled award.

(g) Conditions on Delivery of Stock. The Company will not be obligated to deliver any shares of Common Stock pursuant to the Plan or to remove restrictions from shares previously issued or delivered under the Plan until (i) all conditions of the Award have been met

or removed to the satisfaction of the Company, (ii) in the opinion of the Company's counsel, all other legal matters in connection with the issuance and delivery of such shares have been satisfied, including any applicable securities laws and regulations and any applicable stock exchange or stock market rules and regulations, and (iii) the Participant has executed and delivered to the Company such representations or agreements as the Company may consider appropriate to satisfy the requirements of any applicable laws, rules or regulations.

(h) Acceleration. The Board may at any time provide that any Award shall become immediately exercisable in whole or in part, free of some or all restrictions or conditions, or otherwise realizable in whole or in part, as the case may be.

11. Miscellaneous.

(a) No Right To Employment or Other Status. No person shall have any claim or right to be granted an Award by virtue of the adoption of the Plan, and the grant of an Award shall not be construed as giving a Participant the right to continued employment or any other relationship with the Company. The Company expressly reserves the right at any time to dismiss or otherwise terminate its relationship with a Participant free from any liability or claim under the Plan, except as expressly provided in the applicable Award.

(b) No Rights As Stockholder. Subject to the provisions of the applicable Award, no Participant or Designated Beneficiary shall have any rights as a stockholder with respect to any shares of Common Stock to be distributed with respect to an Award until becoming the record holder of such shares.

(c) Effective Date and Term of Plan. The Plan shall become effective on the date on which it is adopted by the Board. No Awards shall be granted under the Plan after the expiration of 10 years from the earlier of (i) the date on which the Plan was adopted by the Board or (ii) the date the Plan was approved by the Company's stockholders, but Awards previously granted may extend beyond that date.

(d) Amendment of Plan. The Board may amend, suspend or terminate the Plan or any portion thereof at any time; *provided* that if at any time the approval of the Company's stockholders is required as to any modification or amendment under Section 422 of the Code or any successor provision with respect to Incentive Stock Options, the Board may not effect such modification or amendment without such approval. Unless otherwise specified in the amendment, any amendment to the Plan adopted in accordance with this Section 11(d) shall apply to, and be binding on the holders of, all Awards outstanding under the Plan at the time the amendment is adopted, provided the Board determines that such amendment, taking into account any related action, does not materially and adversely affect the rights of Participants under the Plan.

(e) Authorization of Sub-Plans (including Grants to non-U.S. Employees). The Board may from time to time establish one or more sub-plans under the Plan for purposes of satisfying applicable securities, tax or other laws of various jurisdictions. The Board shall establish such sub-plans by adopting supplements to the Plan containing (i) such limitations on the Board's discretion under the Plan as the Board deems necessary or desirable or (ii) such

additional terms and conditions not otherwise inconsistent with the Plan as the Board shall deem necessary or desirable. All supplements adopted by the Board shall be deemed to be part of the Plan, but each supplement shall apply only to Participants within the affected jurisdiction and the Company shall not be required to provide copies of any supplement to Participants in any jurisdiction which is not the subject of such supplement.

(f) Compliance with Section 409A of the Code. Except as provided in individual Award agreements initially or by amendment, if and to the extent (i) any portion of any payment, compensation or other benefit provided to a Participant pursuant to the Plan in connection with Participant's employment termination constitutes "nonqualified deferred compensation" within the meaning of Section 409A of the Code and (ii) the Participant is a specified employee as defined in Section 409A(a)(2)(B)(i) of the Code, in each case as determined by the Company in accordance with its procedures, by which determinations the Participant (through accepting the Award) agrees that the Participant is bound, such portion of the payment, compensation or other benefit shall not be paid before the day that is six months plus one day after the date of "separation from service" (as determined under Section 409A of the Code) (the "**New Payment Date**"), except as Section 409A of the Code may then permit. The aggregate of any payments that otherwise would have been paid to the Participant during the period between the date of separation from service and the New Payment Date shall be paid to the Participant in a lump sum on such New Payment Date, and any remaining payments will be paid on their original schedule.

The Company makes no representations or warranty and shall have no liability to the Participant or any other person if any provisions of or payments, compensation or other benefits under the Plan are determined to constitute nonqualified deferred compensation subject to Section 409A of the Code but do not to satisfy the conditions of that section.

(g) Limitations on Liability. Notwithstanding any other provisions of the Plan, no individual acting as a director, officer, other employee, or agent of the Company will be liable to any Participant, former Participant, spouse, beneficiary, or any other person for any claim, loss, liability, or expense incurred in connection with the Plan, nor will such individual be personally liable with respect to the Plan because of any contract or other instrument such individual executes in such individual's capacity as a director, officer, other employee, or agent of the Company. The Company will indemnify and hold harmless each director, officer, other employee, or agent of the Company to whom any duty or power relating to the administration or interpretation of the Plan has been or will be delegated, against any cost or expense (including attorneys' fees) or liability (including any sum paid in settlement of a claim with the Board's approval) arising out of any act or omission to act concerning the Plan unless arising out of such person's own fraud or bad faith.

(h) Governing Law. The provisions of the Plan and all Awards made hereunder shall be governed by and interpreted in accordance with the laws of the State of Delaware, excluding choice-of-law principles of the law of such state that would require the application of the laws of a jurisdiction other than the State of Delaware.

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CALIFORNIA SUPPLEMENT

Pursuant to Section 11(e) of the Plan, the Board has adopted this supplement for purposes of satisfying the requirements of Section 25102(o) of the California Law:

Any Awards granted under the Plan to a Participant who is a resident of the State of California on the date of grant (a “**California Participant**”) shall be subject to the following additional limitations, terms and conditions:

1. Additional Limitations on Options.

(a) Maximum Duration of Options. No Options granted to California Participants shall have a term in excess of 10 years measured from the Option grant date.

(b) Minimum Exercise Period Following Termination. Unless a California Participant’s employment is terminated for cause (as defined by applicable law, the terms of the Plan or option grant or a contract of employment), in the event of termination of employment of such Participant, such Participant shall have the right to exercise an Option, to the extent that such Participant is entitled to exercise such Option on the date employment terminated, until the earlier of: (i) at least six months from the date of termination, if termination was caused by such Participant’s death or disability, (ii) at least 30 days from the date of termination, if termination was caused other than by such Participant’s death or disability and (iii) the Option expiration date.

2. Additional Limitations for Other Stock-Based Awards. The terms of all Awards granted to a California Participant under Section 8 of the Plan shall comply, to the extent applicable, with Sections 260.140.42, 260.140.45 and 260.140.46 of the California Code of Regulations.

3. Additional Limitations on Timing of Awards. No Award granted to a California Participant shall become exercisable, vested or realizable, as applicable to such Award, unless the Plan has been approved by the holders of a majority of the Company’s outstanding voting securities by the later of (i) within 12 months before or after the date the Plan was adopted by the Board, or (ii) prior to or within 12 months of the granting of any Award to a California Participant.

4. Additional Restriction Regarding Recapitalizations, Stock Splits, Etc. For purposes of Section 9 of the Plan, in the event of a stock split, reverse stock split, stock dividend, recapitalization, combination, reclassification or other distribution of the Company’s securities underlying the Award without the receipt of consideration by the Company, the number of securities purchasable, and in the case of Options, the exercise price of such Options, must be proportionately adjusted.

5. Additional Limitations on Transferability of Awards. Notwithstanding the provisions of Section 10(a) of the Plan, an Award granted to a California Participant may not be transferred to an executor or guardian upon the disability of the Participant.

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FULCRUM THERAPEUTICS

INCENTIVE STOCK OPTION AGREEMENT
GRANTED UNDER 2016 STOCK INCENTIVE PLAN1. Grant of Option.

This Incentive Stock Option Agreement (the “**Agreement**”) evidences the grant by Fulcrum Therapeutics, Inc., a Delaware corporation (the “**Company**”), on [], 20 [] (the “**Grant Date**”) to [], an employee of the Company (the “**Participant**”), of an option to purchase, in whole or in part, on the terms provided herein and in the Company’s 2016 Stock Incentive Plan (the “**Plan**”), a total of [] shares (the “**Shares**”) of common stock, \$0.001 par value per share, of the Company (“**Common Stock**”) at \$[] per Share. Unless earlier terminated, this option shall expire at 5:00 p.m., Eastern time, on [], 20 [] [date is ten years minus one day from grant date] (the “**Final Exercise Date**”).

It is intended that the option evidenced by this Agreement shall be an incentive stock option as defined in Section 422 of the Internal Revenue Code of 1986, as amended, and any regulations promulgated thereunder (the “**Code**”). To the extent not designated as an incentive stock option, or to the extent that the option does not qualify as an incentive stock option, the option shall be a nonstatutory stock option. Except as otherwise indicated by the context, the term “**Participant**”, as used in this option, shall be deemed to include any person who acquires the right to exercise this option validly under its terms.

2. Vesting Schedule.

This option will become exercisable (“**vest**”) as to []. For purposes of this Agreement, “**Vesting Commencement Date**” shall mean [].

The right of exercise shall be cumulative so that to the extent the option is not exercised in any period to the maximum extent permissible it shall continue to be exercisable, in whole or in part, with respect to all Shares for which it is vested until the earlier of the Final Exercise Date or the termination of this option under Section 3 hereof or the Plan.

3. Exercise of Option.

(a) Form of Exercise. Each election to exercise this option shall be accompanied by a completed Notice of Stock Option Exercise in the form attached hereto as Exhibit A, signed by the Participant, and received by the Company at its principal office, accompanied by this Agreement, and payment in full in the manner provided in the Plan. The Participant may purchase less than the number of Shares covered hereby, provided that no partial exercise of this option may be for any fractional share or for fewer than ten whole shares.

(b) Continuous Relationship with the Company Required. Except as otherwise provided in this Section 3, this option may not be exercised unless the Participant, at the time he or she exercises this option, is, and has been at all times since the Grant Date, an employee or

officer of, or consultant or advisor to, the Company or any parent or subsidiary of the Company as defined in Section 424(e) or (f) of the Code (an “**Eligible Participant**”).

(c) Termination of Relationship with the Company. If the Participant ceases to be an Eligible Participant for any reason, then, except as provided in paragraphs (d) and (e) below, the right to exercise this option shall terminate three months after such cessation (but in no event after the Final Exercise Date), provided that this option shall be exercisable only to the extent that the Participant was entitled to exercise this option on the date of such cessation. Notwithstanding the foregoing, if the Participant, prior to the Final Exercise Date, violates the non-competition or confidentiality provisions of any employment contract, confidentiality and nondisclosure agreement or other agreement between the Participant and the Company, the right to exercise this option shall terminate immediately upon such violation.

(d) Exercise Period Upon Death or Disability. If the Participant dies or becomes disabled (within the meaning of Section 22(e)(3) of the Code) prior to the Final Exercise Date while he or she is an Eligible Participant and the Company has not terminated such relationship for “cause” as specified in paragraph (e) below, this option shall be exercisable, within the period of one year following the date of death or disability of the Participant, by the Participant (or in the case of death by an authorized transferee), provided that this option shall be exercisable only to the extent that this option was exercisable by the Participant on the date of his or her death or disability, and further provided that this option shall not be exercisable after the Final Exercise Date.

(e) Termination for Cause. If, prior to the Final Exercise Date, the Participant’s employment is terminated by the Company for Cause (as defined below), the right to exercise this option shall terminate immediately upon the effective date of such termination of employment. If, prior to the Final Exercise Date, the Participant is given notice by the Company of the termination of his or her employment by the Company for Cause, and the effective date of such employment termination is subsequent to the date of delivery of such notice, the right to exercise this option shall be suspended from the time of the delivery of such notice until the earlier of (i) such time as it is determined or otherwise agreed that the Participant’s employment shall not be terminated for Cause as provided in such notice or (ii) the effective date of such termination of employment (in which case the right to exercise this option shall, pursuant to the preceding sentence, terminate upon the effective date of such termination of employment). If the Participant is party to an employment or severance agreement with the Company that contains a definition of “cause” for termination of employment, “Cause” shall have the meaning ascribed to such term in such agreement. Otherwise, “Cause” shall mean willful misconduct by the Participant or willful failure by the Participant to perform his or her responsibilities to the Company (including, without limitation, breach by the Participant of any provision of any employment, consulting, advisory, nondisclosure, non-competition or other similar agreement between the Participant and the Company), as determined by the Company, which determination shall be conclusive. The Participant’s employment shall be considered to have been terminated for Cause if the Company determines, within 30 days after the Participant’s resignation, that termination for Cause was warranted.

4. Company Right of First Refusal.

(a) Notice of Proposed Transfer. If the Participant proposes to sell, assign, transfer, pledge, hypothecate or otherwise dispose of, by operation of law or otherwise (collectively, “transfer”) any Shares acquired upon exercise of this option, then the Participant shall first give written notice of the proposed transfer (the “**Transfer Notice**”) to the Company. The Transfer Notice shall name the proposed transferee and state the number of such Shares the Participant proposes to transfer (the “**Offered Shares**”), the price per share and all other material terms and conditions of the transfer.

(b) Company Right to Purchase. For 30 days following its receipt of such Transfer Notice, the Company shall have the option to purchase all or part of the Offered Shares at the price and upon the terms set forth in the Transfer Notice. In the event the Company elects to purchase all or part of the Offered Shares, it shall give written notice of such election to the Participant within such 30-day period. Within 10 days after his or her receipt of such notice, the Participant shall tender to the Company at its principal offices the certificate or certificates representing the Offered Shares to be purchased by the Company, duly endorsed in blank by the Participant or with duly endorsed stock powers attached thereto, all in a form suitable for transfer of the Offered Shares to the Company. Promptly following receipt of such certificate or certificates, the Company shall deliver or mail to the Participant a check in payment of the purchase price for such Offered Shares; provided that if the terms of payment set forth in the Transfer Notice were other than cash against delivery, the Company may pay for the Offered Shares on the same terms and conditions as were set forth in the Transfer Notice; and provided further that any delay in making such payment shall not invalidate the Company’s exercise of its option to purchase the Offered Shares.

(c) Shares Not Purchased By Company. If the Company does not elect to acquire all of the Offered Shares, the Participant may, within the 30-day period following the expiration of the option granted to the Company under subsection (b) above, transfer the Offered Shares which the Company has not elected to acquire to the proposed transferee, provided that such transfer shall not be on terms and conditions more favorable to the transferee than those contained in the Transfer Notice. Notwithstanding any of the above, all Offered Shares transferred pursuant to this Section 4 shall remain subject to the right of first refusal set forth in this Section 4 and such transferee shall, as a condition to such transfer, deliver to the Company a written instrument confirming that such transferee shall be bound by all of the terms and conditions of this Section 4.

(d) Consequences of Non-Delivery. After the time at which the Offered Shares are required to be delivered to the Company for transfer to the Company pursuant to subsection (b) above, the Company shall not pay any dividend to the Participant on account of such Offered Shares or permit the Participant to exercise any of the privileges or rights of a stockholder with respect to such Offered Shares, but shall, insofar as permitted by law, treat the Company as the owner of such Offered Shares.

(e) Exempt Transactions. The following transactions shall be exempt from the provisions of this Section 4:

- (1) any transfer of Shares to or for the benefit of any spouse, child or grandchild of the Participant, or to a trust for their benefit;
- (2) any transfer pursuant to an effective registration statement filed by the Company under the Securities Act of 1933, as amended (the “**Securities Act**”); and
- (3) the sale of all or substantially all of the outstanding shares of capital stock of the Company (including pursuant to a merger or consolidation);

provided, however, that in the case of a transfer pursuant to clause (1) above, such Shares shall remain subject to the right of first refusal set forth in this Section 4.

(f) Assignment of Company Right. The Company may assign its rights to purchase Offered Shares in any particular transaction under this Section 4 to one or more persons or entities.

(g) Termination. The provisions of this Section 4 shall terminate upon the earlier of the following events:

(1) the closing of the sale of shares of Common Stock in an underwritten public offering pursuant to an effective registration statement filed by the Company under the Securities Act; or

(2) the sale of all or substantially all of the outstanding shares of capital stock, assets or business of the Company, by merger, consolidation, sale of assets or otherwise (other than a merger or consolidation in which all or substantially all of the individuals and entities who were beneficial owners of the Company’s voting securities immediately prior to such transaction beneficially own, directly or indirectly, more than 75% (determined on an as-converted basis) of the outstanding securities entitled to vote generally in the election of directors of the resulting, surviving or acquiring corporation in such transaction).

(h) No Obligation to Recognize Invalid Transfer. The Company shall not be required (1) to transfer on its books any of the Shares which shall have been sold or transferred in violation of any of the provisions set forth in this Section 4, or (2) to treat as owner of such Shares or to pay dividends to any transferee to whom any such Shares shall have been so sold or transferred.

(i) Legends. The certificate representing Shares shall bear a legend substantially in the following form (in addition to, or in combination with, any legend required by applicable federal and state securities laws and agreements relating to the transfer of the Company securities):

“The shares represented by this certificate are subject to a right of first refusal in favor of the Company, as provided in a certain stock option agreement with the Company.”

5. Agreement in Connection with Initial Public Offering.

The Participant agrees, in connection with the initial underwritten public offering of the Common Stock pursuant to a registration statement under the Securities Act, (i) not to (a) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares of Common Stock or any other securities of the Company or (b) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of shares of Common Stock or other securities of the Company, whether any transaction described in clause (a) or (b) is to be settled by delivery of securities, in cash or otherwise, during the period beginning on the date of the filing of such registration statement with the Securities and Exchange Commission and ending 180 days after the date of the final prospectus relating to the offering (plus up to an additional 34 days to the extent requested by the managing underwriters for such offering in order to address NASD Rule 2711(f)(4) or NYSE Rule 472(f)(4) or any similar successor provision), and (ii) to execute any agreement reflecting clause (i) above as may be requested by the Company or the managing underwriters at the time of such offering. The Company may impose stop-transfer instructions with respect to the shares of Common Stock or other securities subject to the foregoing restriction until the end of the “lock-up” period.

6. Tax Matters.

(a) Withholding. No Shares will be issued pursuant to the exercise of this option unless and until the Participant pays to the Company, or makes provision satisfactory to the Company for payment of, any federal, state or local withholding taxes required by law to be withheld in respect of this option.

(b) Disqualifying Disposition. If this option satisfies the requirements to be treated as an incentive stock option under the Code and the Participant disposes of Shares acquired upon exercise of this option within two years from the Grant Date or one year after such Shares were acquired pursuant to exercise of this option, the Participant shall notify the Company in writing of such disposition.

7. Transfer Restrictions.

(a) This option may not be sold, assigned, transferred, pledged or otherwise encumbered by the Participant, either voluntarily or by operation of law, except by will or the laws of descent and distribution, and, during the lifetime of the Participant, this option shall be exercisable only by the Participant.

(b) The Participant agrees that he or she will not transfer any Shares issued pursuant to the exercise of this option unless the transferee, as a condition to such transfer, delivers to the Company a written instrument confirming that such transferee shall be bound by all of the terms and conditions of Section 4 and Section 5; provided that such a written confirmation shall not be required with respect to (1) Section 4 after such provision has terminated in accordance with Section 4(g) or (2) Section 5 after the completion of the lock-up period in connection with the Company’s initial underwritten public offering.

8. Provisions of the Plan.

This option is subject to the provisions of the Plan (including the provisions relating to amendments to the Plan), a copy of which is furnished to the Participant with this option.

[Remainder of Page Intentionally Left Blank]

IN WITNESS WHEREOF, the parties hereto have executed this Agreement as of the day and year first above written. The Participant hereby accepts the foregoing option and agrees to the terms and conditions thereof. The Participant hereby acknowledges receipt of a copy of the Company's 2016 Stock Incentive Plan.

COMPANY:

Fulcrum Therapeutics, Inc.

By: _____
Name: _____
Title: _____

PARTICIPANT:

By: _____
[Name]
Address: []
[]

SPOUSAL CONSENT:

By: _____
Name: _____
Address: []
[]

SIGNATURE PAGE TO INCENTIVE STOCK OPTION AGREEMENT

EXHIBIT A

NOTICE OF STOCK OPTION EXERCISE

[DATE]

Fulcrum Therapeutics, Inc.
[Address]
[Address]

Attention: Treasurer

Dear Sir or Madam:

I am the holder of a [] Stock Option granted to me under the Fulcrum Therapeutics, Inc. (the “**Company**”) 2016 Stock Incentive Plan on [] for the purchase of [] shares of Common Stock of the Company at a purchase price of \$[] per share.

I hereby exercise my option to purchase [] shares of Common Stock (the “**Shares**”), for which I have enclosed [] in the amount of []. Please register my stock certificate as follows:

Name(s):

Address:

I represent, warrant and covenant as follows:

1. I am purchasing the Shares for my own account for investment only, and not with a view to, or for sale in connection with, any distribution of the Shares in violation of the Securities Act of 1933 (the “**Securities Act**”), or any rule or regulation under the Securities Act.
 2. I have had such opportunity as I have deemed adequate to obtain from representatives of the Company such information as is necessary to permit me to evaluate the merits and risks of my investment in the Company.
 3. I have sufficient experience in business, financial and investment matters to be able to evaluate the risks involved in the purchase of the Shares and to make an informed investment decision with respect to such purchase.
 4. I can afford a complete loss of the value of the Shares and am able to bear the economic risk of holding such Shares for an indefinite period.
-

5. I understand that (i) the Shares have not been registered under the Securities Act and are “restricted securities” within the meaning of Rule 144 under the Securities Act, (ii) the Shares cannot be sold, transferred or otherwise disposed of unless they are subsequently registered under the Securities Act or an exemption from registration is then available; (iii) in any event, the exemption from registration under Rule 144 will not be available for at least one year and even then will not be available unless a public market then exists for the Common Stock, adequate information concerning the Company is then available to the public, and other terms and conditions of Rule 144 are complied with; and (iv) there is now no registration statement on file with the Securities and Exchange Commission with respect to any stock of the Company and the Company has no obligation or current intention to register the Shares under the Securities Act.

Very truly yours,

[Name]

FULCRUM THERAPEUTICS, INC.

NONSTATUTORY STOCK OPTION AGREEMENT
GRANTED UNDER 2016 STOCK INCENTIVE PLAN1. Grant of Option.

This Nonstatutory Stock Option Agreement (the “**Agreement**”) evidences the grant by Fulcrum Therapeutics, Inc., a Delaware corporation (the “**Company**”), on [], 20 [] (the “**Grant Date**”) to [], an employee, consultant or director of the Company (the “**Participant**”), of an option to purchase, in whole or in part, on the terms provided herein and in the Company’s 2016 Stock Incentive Plan (the “**Plan**”), a total of [] shares (the “**Shares**”) of common stock, \$0.0001 par value per share, of the Company (“**Common Stock**”) at \$[] per Share. Unless earlier terminated, this option shall expire at 5:00 p.m., Eastern time, on [], 20 [] [date is ten years minus one day from grant date] (the “**Final Exercise Date**”).

It is intended that the option evidenced by this Agreement shall not be an incentive stock option as defined in Section 422 of the Internal Revenue Code of 1986, as amended, and any regulations promulgated thereunder (the “**Code**”). Except as otherwise indicated by the context, the term “**Participant**”, as used in this option, shall be deemed to include any person who acquires the right to exercise this option validly under its terms.

2. Vesting Schedule.

This option will become exercisable (“**vest**”) as to []. For purposes of this Agreement, “**Vesting Commencement Date**” shall mean [].

The right of exercise shall be cumulative so that to the extent the option is not exercised in any period to the maximum extent permissible it shall continue to be exercisable, in whole or in part, with respect to all Shares for which it is vested until the earlier of the Final Exercise Date or the termination of this option under Section 3 hereof or the Plan.

3. Exercise of Option.

(a) Form of Exercise. Each election to exercise this option shall be accompanied by a completed Notice of Stock Option Exercise in the form attached hereto as Exhibit A, signed by the Participant, and received by the Company at its principal office, accompanied by this Agreement, and payment in full in the manner provided in the Plan. The Participant may purchase less than the number of Shares covered hereby, provided that no partial exercise of this option may be for any fractional share or for fewer than ten whole shares.

(b) Continuous Relationship with the Company Required. Except as otherwise provided in this Section 3, this option may not be exercised unless the Participant, at the time he or she exercises this option, is, and has been at all times since the Grant Date, an employee, officer or director of, or consultant or advisor to, the Company or any other entity the employees,

officers, directors, consultants, or advisors of which are eligible to receive option grants under the Plan (an “**Eligible Participant**”).

(c) Termination of Relationship with the Company. If the Participant ceases to be an Eligible Participant for any reason, then, except as provided in paragraphs (d) and (e) below, the right to exercise this option shall terminate three months after such cessation (but in no event after the Final Exercise Date), provided that this option shall be exercisable only to the extent that the Participant was entitled to exercise this option on the date of such cessation. Notwithstanding the foregoing, if the Participant, prior to the Final Exercise Date, violates the non-competition or confidentiality provisions of any employment contract, confidentiality and nondisclosure agreement or other agreement between the Participant and the Company, the right to exercise this option shall terminate immediately upon such violation.

(d) Exercise Period Upon Death or Disability. If the Participant dies or becomes disabled (within the meaning of Section 22(e)(3) of the Code) prior to the Final Exercise Date while he or she is an Eligible Participant and the Company has not terminated such relationship for “cause” as specified in paragraph (e) below, this option shall be exercisable, within the period of one year following the date of death or disability of the Participant, by the Participant (or in the case of death by an authorized transferee), provided that this option shall be exercisable only to the extent that this option was exercisable by the Participant on the date of his or her death or disability, and further provided that this option shall not be exercisable after the Final Exercise Date.

(e) Termination for Cause. If, prior to the Final Exercise Date, the Participant’s employment or other relationship with the Company is terminated by the Company for Cause (as defined below), the right to exercise this option shall terminate immediately upon the effective date of such termination of employment or other relationship. If, prior to the Final Exercise Date, the Participant is given notice by the Company of the termination of his or her employment or other relationship by the Company for Cause, and the effective date of such employment or other termination is subsequent to the date of the delivery of such notice, the right to exercise this option shall be suspended from the time of the delivery of such notice until the earlier of (i) such time as it is determined or otherwise agreed that the Participant’s employment or other relationship shall not be terminated for Cause as provided in such notice or (ii) the effective date of such termination of employment or other relationship (in which case the right to exercise this option shall, pursuant to the preceding sentence, terminate immediately upon the effective date of such termination of employment or other relationship). If the Participant is party to an employment, consulting or severance agreement with the Company that contains a definition of “cause” for termination of employment or other relationship, “Cause” shall have the meaning ascribed to such term in such agreement. Otherwise, “Cause” shall mean willful misconduct by the Participant or willful failure by the Participant to perform his or her responsibilities to the Company (including, without limitation, breach by the Participant of any provision of any employment, consulting, advisory, nondisclosure, non-competition or other similar agreement between the Participant and the Company), as determined by the Company, which determination shall be conclusive. The Participant’s employment or other relationship shall be considered to have been terminated for “Cause” if the Company determines, within 30 days after the Participant’s resignation, that termination for Cause was warranted.

4. Company Right of First Refusal.

(a) Notice of Proposed Transfer. If the Participant proposes to sell, assign, transfer, pledge, hypothecate or otherwise dispose of, by operation of law or otherwise (collectively, “transfer”) any Shares acquired upon exercise of this option, then the Participant shall first give written notice of the proposed transfer (the “**Transfer Notice**”) to the Company. The Transfer Notice shall name the proposed transferee and state the number of such Shares the Participant proposes to transfer (the “**Offered Shares**”), the price per share and all other material terms and conditions of the transfer.

(b) Company Right to Purchase. For 30 days following its receipt of such Transfer Notice, the Company shall have the option to purchase all or part of the Offered Shares at the price and upon the terms set forth in the Transfer Notice. In the event the Company elects to purchase all or part of the Offered Shares, it shall give written notice of such election to the Participant within such 30-day period. Within 10 days after his or her receipt of such notice, the Participant shall tender to the Company at its principal offices the certificate or certificates representing the Offered Shares to be purchased by the Company, duly endorsed in blank by the Participant or with duly endorsed stock powers attached thereto, all in a form suitable for transfer of the Offered Shares to the Company. Promptly following receipt of such certificate or certificates, the Company shall deliver or mail to the Participant a check in payment of the purchase price for such Offered Shares; provided that if the terms of payment set forth in the Transfer Notice were other than cash against delivery, the Company may pay for the Offered Shares on the same terms and conditions as were set forth in the Transfer Notice; and provided further that any delay in making such payment shall not invalidate the Company’s exercise of its option to purchase the Offered Shares.

(c) Shares Not Purchased By Company. If the Company does not elect to acquire all of the Offered Shares, the Participant may, within the 30-day period following the expiration of the option granted to the Company under subsection (b) above, transfer the Offered Shares which the Company has not elected to acquire to the proposed transferee, provided that such transfer shall not be on terms and conditions more favorable to the transferee than those contained in the Transfer Notice. Notwithstanding any of the above, all Offered Shares transferred pursuant to this Section 4 shall remain subject to the right of first refusal set forth in this Section 4 and such transferee shall, as a condition to such transfer, deliver to the Company a written instrument confirming that such transferee shall be bound by all of the terms and conditions of this Section 4.

(d) Consequences of Non-Delivery. After the time at which the Offered Shares are required to be delivered to the Company for transfer to the Company pursuant to subsection (b) above, the Company shall not pay any dividend to the Participant on account of such Offered Shares or permit the Participant to exercise any of the privileges or rights of a stockholder with respect to such Offered Shares, but shall, insofar as permitted by law, treat the Company as the owner of such Offered Shares.

(e) Exempt Transactions. The following transactions shall be exempt from the provisions of this Section 4:

- (1) any transfer of Shares to or for the benefit of any spouse, child or grandchild of the Participant, or to a trust for their benefit;
- (2) any transfer pursuant to an effective registration statement filed by the Company under the Securities Act of 1933, as amended (the “**Securities Act**”); and
- (3) the sale of all or substantially all of the outstanding shares of capital stock of the Company (including pursuant to a merger or consolidation);

provided, however, that in the case of a transfer pursuant to clause (1) above, such Shares shall remain subject to the right of first refusal set forth in this Section 4.

(f) Assignment of Company Right. The Company may assign its rights to purchase Offered Shares in any particular transaction under this Section 4 to one or more persons or entities.

(g) Termination. The provisions of this Section 4 shall terminate upon the earlier of the following events:

(1) the closing of the sale of shares of Common Stock in an underwritten public offering pursuant to an effective registration statement filed by the Company under the Securities Act; or

(2) the sale of all or substantially all of the outstanding shares of capital stock, assets or business of the Company, by merger, consolidation, sale of assets or otherwise (other than a merger or consolidation in which all or substantially all of the individuals and entities who were beneficial owners of the Company’s voting securities immediately prior to such transaction beneficially own, directly or indirectly, more than 75% (determined on an as-converted basis) of the outstanding securities entitled to vote generally in the election of directors of the resulting, surviving or acquiring corporation in such transaction).

(h) No Obligation to Recognize Invalid Transfer. The Company shall not be required (1) to transfer on its books any of the Shares which shall have been sold or transferred in violation of any of the provisions set forth in this Section 4, or (2) to treat as owner of such Shares or to pay dividends to any transferee to whom any such Shares shall have been so sold or transferred.

(i) Legends. The certificate representing Shares shall bear a legend substantially in the following form (in addition to, or in combination with, any legend required by applicable federal and state securities laws and agreements relating to the transfer of the Company securities):

“The shares represented by this certificate are subject to a right of first refusal in favor of the Company, as provided in a certain stock option agreement with the Company.”

5. Agreement in Connection with Initial Public Offering.

The Participant agrees, in connection with the initial underwritten public offering of the Common Stock pursuant to a registration statement under the Securities Act, (i) not to (a) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares of Common Stock or any other securities of the Company or (b) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of shares of Common Stock or other securities of the Company, whether any transaction described in clause (a) or (b) is to be settled by delivery of securities, in cash or otherwise, during the period beginning on the date of the filing of such registration statement with the Securities and Exchange Commission and ending 180 days after the date of the final prospectus relating to the offering (plus up to an additional 34 days to the extent requested by the managing underwriters for such offering in order to address NASD Rule 2711(f)(4) or NYSE Rule 472(f)(4) or any similar successor provision), and (ii) to execute any agreement reflecting clause (i) above as may be requested by the Company or the managing underwriters at the time of such offering. The Company may impose stop-transfer instructions with respect to the shares of Common Stock or other securities subject to the foregoing restriction until the end of the “lock-up” period.

6. Withholding.

No Shares will be issued pursuant to the exercise of this option unless and until the Participant pays to the Company, or makes provision satisfactory to the Company for payment of, any federal, state or local withholding taxes required by law to be withheld in respect of this option.

7. Transfer Restrictions.

(a) This option may not be sold, assigned, transferred, pledged or otherwise encumbered by the Participant, either voluntarily or by operation of law, except by will or the laws of descent and distribution, and, during the lifetime of the Participant, this option shall be exercisable only by the Participant.

(b) The Participant agrees that he or she will not transfer any Shares issued pursuant to the exercise of this option unless the transferee, as a condition to such transfer, delivers to the Company a written instrument confirming that such transferee shall be bound by all of the terms and conditions of Section 4 and Section 5; provided that such a written confirmation shall not be required with respect to (1) Section 4 after such provision has terminated in accordance with Section 4(g) or (2) Section 5 after the completion of the lock-up period in connection with the Company’s initial underwritten public offering.

8. Provisions of the Plan.

This option is subject to the provisions of the Plan (including the provisions relating to amendments to the Plan), a copy of which is furnished to the Participant with this option.

[Remainder of Page Intentionally Left Blank]

IN WITNESS WHEREOF, the parties hereto have executed this Agreement as of the day and year first above written. The Participant hereby accepts the foregoing option and agrees to the terms and conditions thereof. The Participant hereby acknowledges receipt of a copy of the Company's 2016 Stock Incentive Plan.

COMPANY:

Fulcrum Therapeutics, Inc.

By: _____
Name: _____
Title: _____

PARTICIPANT:

By: _____
[Name]
Address: []
[]

SPOUSAL CONSENT: (1)

By: _____
Name: _____
Address: []
[]

(1) If the Participant resides in a community property state, it is desirable to have the Participant's spouse also accept the option. The following are community property states: Arizona, California, Idaho, Louisiana, Nevada, New Mexico, Texas, and Washington. Although Wisconsin is not formally a community property state, it has laws governing the division of marital property similar to community property states and it may be desirable to have a Wisconsin Participant's spouse accept the option.

EXHIBIT A

NOTICE OF STOCK OPTION EXERCISE

[DATE](1)

Fulcrum Therapeutics, Inc.

[Address]

[Address]

Attention: Treasurer

Dear Sir or Madam:

I am the holder of a Nonstatutory Stock Option granted to me under the Fulcrum Therapeutics, Inc. (the "**Company**") 2016 Stock Incentive Plan on [](2) for the purchase of [](3) shares of Common Stock of the Company at a purchase price of \$[](4) per share.

I hereby exercise my option to purchase [](5) shares of Common Stock (the "**Shares**"), for which I have enclosed [](6) in the amount of [](7). Please register my stock certificate as follows:

Name(s): _____ (8)

Address: _____

-
- (1) Enter date of exercise.
 - (2) Enter the date of grant.
 - (3) Enter the total number of shares of Common Stock for which the option was granted.
 - (4) Enter the option exercise price per share of Common Stock.
 - (5) Enter the number of shares of Common Stock to be purchased upon exercise of all or part of the option.
 - (6) Enter "cash", "personal check" or if permitted by the option or Plan, "stock certificates No. XXXX and XXXX".
 - (7) Enter the dollar amount (price per share of Common Stock times the number of shares of Common Stock to be purchased), or the number of shares tendered. Fair market value of shares tendered, together with cash or check, must cover the purchase price of the shares issued upon exercise.
 - (8) Enter name(s) to appear on stock certificate in one of the following formats: (a) your name only (i.e., John Doe); (b) your name and other name (i.e., John Doe and Jane Doe, Joint Tenants with Right to Survivorship); or for Nonstatutory Stock Options only, (c) a child's name, with you as custodian (i.e. Jane Doe, Custodian for Tommy Doe). Note: There may be income and/or gift tax consequences for registering shares in a child's name.
-

I represent, warrant and covenant as follows:

1. I am purchasing the Shares for my own account for investment only, and not with a view to, or for sale in connection with, any distribution of the Shares in violation of the Securities Act of 1933 (the “**Securities Act**”), or any rule or regulation under the Securities Act.
2. I have had such opportunity as I have deemed adequate to obtain from representatives of the Company such information as is necessary to permit me to evaluate the merits and risks of my investment in the Company.
3. I have sufficient experience in business, financial and investment matters to be able to evaluate the risks involved in the purchase of the Shares and to make an informed investment decision with respect to such purchase.
4. I can afford a complete loss of the value of the Shares and am able to bear the economic risk of holding such Shares for an indefinite period.
5. I understand that (i) the Shares have not been registered under the Securities Act and are “restricted securities” within the meaning of Rule 144 under the Securities Act, (ii) the Shares cannot be sold, transferred or otherwise disposed of unless they are subsequently registered under the Securities Act or an exemption from registration is then available; (iii) in any event, the exemption from registration under Rule 144 will not be available for at least one year and even then will not be available unless a public market then exists for the Common Stock, adequate information concerning the Company is then available to the public, and other terms and conditions of Rule 144 are complied with; and (iv) there is now no registration statement on file with the Securities and Exchange Commission with respect to any stock of the Company and the Company has no obligation or current intention to register the Shares under the Securities Act.

Very truly yours,

[Name]

FULCRUM THERAPEUTICS, INC.**RESTRICTED STOCK AGREEMENT
GRANTED UNDER 2016 STOCK INCENTIVE PLAN**

This Restricted Stock Agreement (the “**Agreement**”) is made this [] day of [], 2016, between Fulcrum Therapeutics, Inc., a Delaware corporation (the “**Company**”), and [] (the “**Participant**”).

For valuable consideration, receipt of which is acknowledged, the parties hereto agree as follows:

1. Purchase of Shares.

The Company shall issue and sell to the Participant, and the Participant shall purchase from the Company, subject to the terms and conditions set forth in this Agreement and in the Company’s 2016 Stock Incentive Plan (the “**Plan**”), [] shares (the “**Shares**”) of common stock, \$0.001 par value, of the Company (“**Common Stock**”), at a purchase price of [\$] per share. The aggregate purchase price for the Shares shall be paid by the Participant by check payable to the order of the Company or such other method as may be acceptable to the Company. Upon receipt by the Company of payment for the Shares, the Company shall issue to the Participant one or more certificates in the name of the Participant for that number of Shares purchased by the Participant. The Participant agrees that the Shares shall be subject to the purchase options set forth in Sections 3 and 6 of this Agreement and the restrictions on transfer set forth in Section 5 of this Agreement.

2. Certain Definitions.

(a) “**Change in Control**” shall mean the sale of all or substantially all of the outstanding shares of capital stock, assets or business of the Company, by merger, consolidation, sale of assets or otherwise (other than a merger or consolidation in which all or substantially all of the individuals and entities who were beneficial owners of the Company’s voting securities immediately prior to such transaction beneficially own, directly or indirectly, more than 50% (determined on an as-converted basis) of the outstanding securities entitled to vote generally in the election of directors of the resulting, surviving or acquiring corporation in such transaction).

(b) “**Service**” shall mean employment by or the provision of services to the Company or a parent or subsidiary thereof as an advisor, officer, consultant or member of the Board of Directors.

(c) “**Vesting Commencement Date**” shall mean [].

3. Purchase Option.

(a) In the event that the Participant ceases to provide Service for any reason or no reason, with or without Cause, prior to the [] anniversary of the Vesting Commencement Date, the Company shall have the right and option (the “**Purchase Option**”) to

purchase from the Participant, for a sum of \$[] per share (the “**Option Price**”), some or all of the Shares as set forth herein.

(b) All of the Shares shall initially be subject to the Purchase Option. The Participant shall acquire a vested interest in, and the Company’s Purchase Option shall accordingly lapse with respect to [].

4. Exercise of Purchase Option and Closing.

(a) The Company may exercise the Purchase Option by delivering or mailing to the Participant (or the Participant’s estate), within 180 days after the termination of the Service of the Participant, a written notice of exercise of the Purchase Option. Such notice shall specify the number of Shares to be purchased. If and to the extent the Purchase Option is not so exercised by the giving of such a notice within such 180-day period, the Purchase Option shall automatically expire and terminate effective upon the expiration of such 180-day period.

(b) Within ten (10) days after delivery to the Participant of the Company’s notice of the exercise of the Purchase Option pursuant to subsection (a) above, the Participant (or the Participant’s estate) shall, pursuant to the provisions of the Joint Escrow Instructions referred to in Section 8 below, tender to the Company at its principal offices the certificate or certificates representing the Shares that the Company has elected to purchase in accordance with the terms of this Agreement, duly endorsed in blank or with duly endorsed stock powers attached thereto, all in form suitable for the transfer of such Shares to the Company. Promptly following its receipt of such certificate or certificates, the Company shall pay to the Participant the aggregate Option Price for such Shares (provided that any delay in making such payment shall not invalidate the Company’s exercise of the Purchase Option with respect to such Shares).

(c) After the time at which any Shares are required to be delivered to the Company for transfer to the Company pursuant to subsection (b) above, the Company shall not pay any dividend to the Participant on account of such Shares or permit the Participant to exercise any of the privileges or rights of a stockholder with respect to such Shares, but shall, in so far as permitted by law, treat the Company as the owner of such Shares.

(d) The Option Price may be payable, at the option of the Company, in cancellation of all or a portion of any outstanding indebtedness of the Participant to the Company or in cash (by check) or both.

(e) The Company shall not purchase any fraction of a Share upon exercise of the Purchase Option, and any fraction of a Share resulting from a computation made pursuant to Section 3 of this Agreement shall be rounded to the nearest whole Share (with any one-half Share being rounded upward).

(f) The Company may assign its Purchase Option to one or more persons or entities.

5. Restrictions on Transfer.

(a) The Participant shall not sell, assign, transfer, pledge, hypothecate or otherwise dispose of, by operation of law or otherwise (collectively “**transfer**”) any Shares, or any interest therein, that are subject to the Purchase Option, except that the Participant may transfer such Shares (i) to or for the benefit of any spouse, children, parents, uncles, aunts, siblings, grandchildren and any other relatives approved by the Board of Directors (collectively, “**Approved Relatives**”) or to a trust established solely for the benefit of the Participant and/or Approved Relatives, provided that such Shares shall remain subject to this Agreement (including without limitation the restrictions on transfer set forth in this Section 5, the Purchase Option and the right of first refusal set forth in Section 6) and such permitted transferee shall, as a condition to such transfer, deliver to the Company a written instrument confirming that such transferee shall be bound by all of the terms and conditions of this Agreement or (ii) as part of the sale of all or substantially all of the shares of capital stock of the Company (including pursuant to a merger or consolidation), provided that, in accordance with the Plan, the securities or other property received by the Participant in connection with such transaction shall remain subject to this Agreement.

(b) The Participant shall not transfer any Shares, or any interest therein, that are no longer subject to the Purchase Option, except in accordance with Section 6 below.

6. Right of First Refusal.

(a) If the Participant proposes to transfer any Shares that are no longer subject to the Purchase Option (either because they are free from the Purchase Option pursuant to Section 3 or because the Purchase Option expired unexercised pursuant to Section 4), then the Participant shall first give written notice of the proposed transfer (the “**Transfer Notice**”) to the Company. The Transfer Notice shall name the proposed transferee and state the number of such Shares the Participant proposes to transfer (the “**Offered Shares**”), the price per share and all other material terms and conditions of the transfer.

(b) For 30 days following its receipt of such Transfer Notice, the Company shall have the option to purchase all or part of the Offered Shares at the price and upon the terms set forth in the Transfer Notice. In the event the Company elects to purchase all or part of the Offered Shares, it shall give written notice of such election to the Participant within such 30-day period. Within 10 days after the Participant’s receipt of such notice, the Participant shall tender to the Company at its principal offices the certificate or certificates representing the Offered Shares to be purchased by the Company, duly endorsed in blank by the Participant or with duly endorsed stock powers attached thereto, all in a form suitable for transfer of the Offered Shares to the Company. Promptly following receipt of such certificate or certificates, the Company shall deliver or mail to the Participant a check in payment of the purchase price for such Offered Shares; provided that if the terms of payment set forth in the Transfer Notice were other than cash against delivery, the Company may pay for the Offered Shares on the same terms and conditions as were set forth in the Transfer Notice; and provided further that any delay in making such payment shall not invalidate the Company’s exercise of its option to purchase the Offered Shares.

(c) If the Company does not elect to acquire all of the Offered Shares, the Participant may, within the 30-day period following the expiration of the option granted to the Company under subsection (b) above, transfer the Offered Shares which the Company has not elected to acquire to the proposed transferee, provided that such transfer shall not be on terms and conditions more favorable to the transferee than those contained in the Transfer Notice. Notwithstanding any of the above, all Offered Shares transferred pursuant to this Section 6 shall remain subject to this Agreement (including without limitation the restrictions on transfer set forth in Section 5 and the right of first refusal set forth in this Section 6) and such transferee shall, as a condition to such transfer, deliver to the Company a written instrument confirming that such transferee shall be bound by all of the terms and conditions of this Agreement.

(d) After the time at which the Offered Shares are required to be delivered to the Company for transfer to the Company pursuant to subsection (b) above, the Company shall not pay any dividend to the Participant on account of such Offered Shares or permit the Participant to exercise any of the privileges or rights of a stockholder with respect to such Offered Shares, but shall, insofar as permitted by law, treat the Company as the owner of such Offered Shares.

(e) The following transactions shall be exempt from the provisions of this Section 6:

(1) a transfer of Shares to or for the benefit of any Approved Relatives, or to a trust established solely for the benefit of the Participant and/or Approved Relatives;

(2) any transfer pursuant to an effective registration statement filed by the Company under the Securities Act of 1933, as amended (the "**Securities Act**"); and

(3) the sale of all or substantially all of the outstanding shares of capital stock of the Company (including pursuant to a merger or consolidation);

provided, however, that in the case of a transfer pursuant to clause (1) above, such Shares shall remain subject to this Agreement (including without limitation the restrictions on transfer set forth in Section 5 and the right of first refusal set forth in this Section 6) and such transferee shall, as a condition to such transfer, deliver to the Company a written instrument confirming that such transferee shall be bound by all of the terms and conditions of this Agreement.

(f) The Company may assign its rights to purchase Offered Shares in any particular transaction under this Section 6 to one or more persons or entities.

(g) The provisions of this Section 6 shall terminate upon the earlier of the following events:

(1) the closing of the sale of shares of Common Stock in an underwritten public offering pursuant to an effective registration statement filed by the Company under the Securities Act; or

(2) a Change in Control.

(h) The Company shall not be required (1) to transfer on its books any of the Shares which shall have been sold or transferred in violation of any of the provisions set forth in this Agreement, or (2) to treat as owner of such Shares or to pay dividends to any transferee to whom any such Shares shall have been so sold or transferred.

7. Agreement in Connection with Initial Public Offering.

The Participant agrees, in connection with the initial underwritten public offering of the Common Stock pursuant to a registration statement under the Securities Act, (i) not to (a) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares of Common Stock or any securities convertible into or exercisable or exchangeable for shares of Common Stock or (b) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of shares of Common Stock, whether any transaction described in clause (a) or (b) is to be settled by delivery of shares of Common Stock or other securities, in cash or otherwise, during the period beginning on the date of the filing of such registration statement with the Securities and Exchange Commission and ending 180 days from the date of the final prospectus relating to the offering (plus up to an additional 34 days to the extent requested by the managing underwriters for such offering in order to address NASD Rule 2711(f)(4) or NYSE Rule 472(f)(4) or any similar successor provision), and (ii) to execute any agreement reflecting clause (i) above as may be requested by the Company or the managing underwriters at the time of such offering. The Company may impose stop-transfer instructions with respect to the shares of Common Stock or other securities subject to the foregoing restriction until the end of the "lock-up" period.

8. Escrow.

The Participant shall, upon the execution of this Agreement, execute Joint Escrow Instructions in the form attached to this Agreement as Exhibit A. The Joint Escrow Instructions shall be delivered to the Secretary of the Company, as escrow agent thereunder. The Participant shall deliver to such escrow agent a stock assignment duly endorsed in blank, in the form attached to this Agreement as Exhibit B, and hereby instructs the Company to deliver to such escrow agent, on behalf of the Participant, the certificate(s) evidencing the Shares issued hereunder. Such materials shall be held by such escrow agent pursuant to the terms of such Joint Escrow Instructions.

9. Restrictive Legends.

All certificates representing Shares shall have affixed thereto legends in substantially the following form, in addition to any other legends that may be required under federal or state securities laws:

"The shares of stock represented by this certificate are subject to restrictions on transfer and an option to purchase set forth in a certain Restricted Stock Agreement between the corporation and the registered owner of these shares (or such owner's predecessor

in interest), and such Agreement is available for inspection without charge at the office of the Secretary of the corporation.”

“The shares represented by this certificate have not been registered under the Securities Act of 1933, as amended, and may not be sold, transferred or otherwise disposed of in the absence of an effective registration statement under such Act or an opinion of counsel satisfactory to the corporation to the effect that such registration is not required.”

10. Provisions of the Plan.

This Agreement is subject to the provisions of the Plan, a copy of which is furnished to the Participant with this Agreement.

11. Investment Representations.

The Participant represents, warrants and covenants as follows:

- (a) The Participant is purchasing the Shares for Participant’s own account for investment only, and not with a view to, or for sale in connection with, any distribution of the Shares in violation of the Securities Act, or any rule or regulation under the Securities Act.
- (b) The Participant has had such opportunity as Participant has deemed adequate to obtain from representatives of the Company such information as is necessary to permit him to evaluate the merits and risks of Participant’s investment in the Company.
- (c) The Participant has sufficient experience in business, financial and investment matters to be able to evaluate the risks involved in the purchase of the Shares and to make an informed investment decision with respect to such purchase.
- (d) The Participant can afford a complete loss of the value of the Shares and is able to bear the economic risk of holding such Shares for an indefinite period.
- (e) The Participant understands that (i) the Shares have not been registered under the Securities Act and are “restricted securities” within the meaning of Rule 144 under the Securities Act; (ii) the Shares cannot be sold, transferred or otherwise disposed of unless they are subsequently registered under the Securities Act or an exemption from registration is then available; (iii) in any event, the exemption from registration under Rule 144 will not be available for at least one year and even then will not be available unless a public market then exists for the Common Stock, adequate information concerning the Company is then available to the public, and other terms and conditions of Rule 144 are complied with; and (iv) there is now no registration statement on file with the Securities and Exchange Commission with respect to any stock of the Company and the Company has no obligation or current intention to register the Shares under the Securities Act.

12. Withholding Taxes; Section 83(b) Election.

(a) The Participant acknowledges and agrees that the Company has the right to deduct from payments of any kind otherwise due to the Participant any federal, state or local taxes of any kind required by law to be withheld with respect to the purchase of the Shares by the Participant or the lapse of the Purchase Option.

(b) The Participant has reviewed with the Participant's own tax advisors the federal, state, local and foreign tax consequences of this investment and the transactions contemplated by this Agreement. The Participant is relying solely on such advisors and not on any statements or representations of the Company or any of its agents. The Participant understands that the Participant (and not the Company) shall be responsible for the Participant's own tax liability that may arise as a result of this investment or the transactions contemplated by this Agreement. The Participant understands that it may be beneficial in many circumstances to elect to be taxed at the time the Shares are granted by the Company rather than when and as the Company's Purchase Option expires by filing an election under Section 83(b) of the Internal Revenue Code of 1986 with the I.R.S. within 30 days from the date of grant by the Company.

THE PARTICIPANT ACKNOWLEDGES THAT IT IS SOLELY THE PARTICIPANT'S RESPONSIBILITY AND NOT THE COMPANY'S TO FILE TIMELY THE ELECTION UNDER SECTION 83(b), EVEN IF THE PARTICIPANT REQUESTS THE COMPANY OR ITS REPRESENTATIVES TO MAKE THIS FILING ON THE PARTICIPANT'S BEHALF.

13. Miscellaneous.

(a) No Rights to Employment. The Participant acknowledges and agrees that the vesting of the Shares pursuant to Section 3 hereof is earned only by the Participant's continuous Service (not through the act of being hired or purchasing the Shares hereunder). The Participant further acknowledges and agrees that the transactions contemplated hereunder and the vesting schedule set forth herein do not constitute an express or implied promise of continued engagement as an employee or consultant for the vesting period, for any period, or at all.

(b) Severability. The invalidity or unenforceability of any provision of this Agreement shall not affect the validity or enforceability of any other provision of this Agreement, and each other provision of this Agreement shall be severable and enforceable to the extent permitted by law.

(c) Waiver. Any provision for the benefit of the Company contained in this Agreement may be waived, either generally or in any particular instance, by the Board of Directors of the Company.

(d) Binding Effect. This Agreement shall be binding upon and inure to the benefit of the Company and the Participant and their respective heirs, executors, administrators, legal representatives, successors and assigns, subject to the restrictions on transfer set forth in Sections 5 and 6 of this Agreement.

(e) Notice. All notices required or permitted hereunder shall be in writing and deemed effectively given upon personal delivery or five days after deposit in the United States Post Office, by registered or certified mail, postage prepaid, addressed to the other party hereto at the address shown beneath his or her or its respective signature to this Agreement, or at such other address or addresses as either party shall designate to the other in accordance with this Section 13(e).

(f) Pronouns. Whenever the context may require, any pronouns used in this Agreement shall include the corresponding masculine, feminine or neuter forms, and the singular form of nouns and pronouns shall include the plural, and vice versa.

(g) Entire Agreement. This Agreement and the Plan constitute the entire agreement between the parties, and supersedes all prior agreements and understandings, relating to the subject matter of this Agreement.

(h) Amendment. This Agreement may be amended or modified only by a written instrument executed by both the Company and the Participant.

(i) Governing Law. This Agreement shall be construed, interpreted and enforced in accordance with the internal laws of the State of Delaware without regard to any applicable conflict of law principles.

(j) Participant's Acknowledgments. The Participant acknowledges that he or she: (i) has read this Agreement; (ii) has been represented in the preparation, negotiation, and execution of this Agreement by legal counsel of the Participant's own choice or has voluntarily declined to seek such counsel; (iii) understands the terms and consequences of this Agreement; (iv) is fully aware of the legal and binding effect of this Agreement; and (v) understands that the law firm of WilmerHale is acting as counsel to the Company in connection with the transactions contemplated by the Agreement, and is not acting as counsel for the Participant.

[Remainder of Page Intentionally Left Blank]

IN WITNESS WHEREOF, the parties hereto have executed the Restricted Stock Agreement as of the date and year first above written. The Participant hereby agrees to the terms and conditions thereof. The Participant hereby acknowledges receipt of a copy of the Company's 2016 Stock Incentive Plan.

COMPANY:

Fulcrum Therapeutics, Inc.

By: _____

Name: _____

Title: _____

Address: [_____]

[_____]

PARTICIPANT:

By: _____

Name: _____

Address: [_____]

[_____]

SPOUSAL CONSENT:

By: _____

Name: _____

Address: [_____]

[_____]

**SIGNATURE PAGE TO RESTRICTED STOCK AGREEMENT
GRANTED UNDER STOCK INCENTIVE PLAN**

JOINT ESCROW INSTRUCTIONS

FULCRUM THERAPEUTICS, INC.
JOINT ESCROW INSTRUCTIONS

[,]

Fulcrum Therapeutics, Inc.

[Address]

[Address]

Attention: Secretary

Dear Secretary:

As Escrow Agent for Fulcrum Therapeutics, Inc., a Delaware corporation (the “**Company**”), and its successors in interest under the Restricted Stock Agreement (the “**Agreement**”) of even date herewith, to which a copy of these Joint Escrow Instructions is attached, and the undersigned person (“**Holder**”), you are hereby authorized and directed to hold the documents delivered to you pursuant to the terms of the Agreement in accordance with the following instructions:

1. Appointment. Holder irrevocably authorizes the Company to deposit with you any certificates evidencing Shares (as defined in the Agreement) to be held by you hereunder and any additions and substitutions to said Shares. For purposes of these Joint Escrow Instructions, “**Shares**” shall be deemed to include any additional or substitute property. Holder does hereby irrevocably constitute and appoint you as his or her attorney-in-fact and agent for the term of this escrow to execute with respect to such Shares all documents necessary or appropriate to make such Shares negotiable and to complete any transaction herein contemplated. Subject to the provisions of this Section 1 and the terms of the Agreement, Holder shall exercise all rights and privileges of a stockholder of the Company while the Shares are held by you.

2. Closing of Purchase.

(a) Upon any purchase by the Company of the Shares pursuant to the Agreement, the Company shall give to Holder and you a written notice specifying the number of Shares to be purchased, the purchase price for the Shares, as determined pursuant to the Agreement, and the time for a closing hereunder (the “**Closing**”) at the principal office of the Company. Holder and the Company hereby irrevocably authorize and direct you to close the transaction contemplated by such notice in accordance with the terms of said notice.

(b) At the Closing, you are directed (i) to date the stock assignment form or forms necessary for the transfer of the Shares, (ii) to fill in on such form or forms the number of Shares being transferred, and (iii) to deliver the same, together with the certificate or certificates evidencing the Shares to be transferred, to the Company against the simultaneous delivery to you of the purchase price for the Shares being purchased pursuant to the Agreement.

3. Withdrawal. The Holder shall have the right to withdraw from this escrow any Shares as to which the Purchase Option (as defined in the Agreement) has terminated or expired.

4. Duties of Escrow Agent.

(a) Your duties hereunder may be altered, amended, modified or revoked only by a writing signed by all of the parties hereto.

(b) You shall be obligated only for the performance of such duties as are specifically set forth herein and may rely and shall be protected in relying or refraining from acting on any instrument reasonably believed by you to be genuine and to have been signed or presented by the proper party or parties. You shall not be personally liable for any act you may do or omit to do hereunder as Escrow Agent or as attorney-in-fact of Holder while acting in good faith and in the exercise of your own good judgment, and any act done or omitted by you pursuant to the advice of your own attorneys shall be conclusive evidence of such good faith.

(c) You are hereby expressly authorized to disregard any and all warnings given by any of the parties hereto or by any other person or entity, excepting only orders or process of courts of law, and are hereby expressly authorized to comply with and obey orders, judgments or decrees of any court. If you are uncertain of any actions to be taken or instructions to be followed, you may refuse to act in the absence of an order, judgment or decrees of a court. In case you obey or comply with any such order, judgment or decree of any court, you shall not be liable to any of the parties hereto or to any other person or entity, by reason of such compliance, notwithstanding any such order, judgment or decree being subsequently reversed, modified, annulled, set aside, vacated or found to have been entered without jurisdiction.

(d) You shall not be liable in any respect on account of the identity, authority or rights of the parties executing or delivering or purporting to execute or deliver the Agreement or any documents or papers deposited or called for hereunder.

(e) You shall be entitled to employ such legal counsel and other experts as you may deem necessary properly to advise you in connection with your obligations hereunder and may rely upon the advice of such counsel.

(f) Your rights and responsibilities as Escrow Agent hereunder shall terminate if (i) you cease to be Secretary of the Company or (ii) you resign by written notice to each party. In the event of a termination under clause (i), your successor as Secretary shall become Escrow Agent hereunder; in the event of a termination under clause (ii), the Company shall appoint a successor Escrow Agent hereunder.

(g) If you reasonably require other or further instruments in connection with these Joint Escrow Instructions or obligations in respect hereto, the necessary parties hereto shall join in furnishing such instruments.

(h) It is understood and agreed that if you believe a dispute has arisen with respect to the delivery and/or ownership or right of possession of the securities held by you hereunder, you are authorized and directed to retain in your possession without liability to anyone all or any part of said securities until such dispute shall have been settled either by mutual written agreement of the parties concerned or by a final order, decree or judgment of a court of competent jurisdiction after the time for appeal has expired and no appeal has been perfected, but you shall be under no duty whatsoever to institute or defend any such proceedings.

(i) These Joint Escrow Instructions set forth your sole duties with respect to any and all matters pertinent hereto and no implied duties or obligations shall be read into these Joint Escrow Instructions against you.

(j) The Company shall indemnify you and hold you harmless against any and all damages, losses, liabilities, costs, and expenses, including attorneys' fees and disbursements, (including without limitation the fees of counsel retained pursuant to Section 4(e) above, for anything done or omitted to be done by you as Escrow Agent in connection with this Agreement or the performance of your duties hereunder, except such as shall result from your gross negligence or willful misconduct.

5. Notice. Any notice required or permitted hereunder shall be given in writing and shall be deemed effectively given upon personal delivery or upon deposit in the United States Post Office, by registered or certified mail with postage and fees prepaid, addressed to each of the other parties thereunto entitled at the following addresses, or at such other addresses as a party may designate by ten days' advance written notice to each of the other parties hereto.

COMPANY: Notices to the Company shall be sent to the address set forth in the salutation hereto, Attn: President

HOLDER: Notices to Holder shall be sent to the address set forth below Holder's signature below.

ESCROW AGENT: Notices to the Escrow Agent shall be sent to the address set forth in the salutation hereto.

6. Miscellaneous.

(a) By signing these Joint Escrow Instructions, you become a party hereto only for the purpose of said Joint Escrow Instructions, and you do not become a party to the Agreement.

(b) This instrument shall be binding upon and inure to the benefit of the parties hereto and their respective successors and permitted assigns.

[Remainder of Page Intentionally Left Blank]

IN WITNESS WHEREOF, the parties hereto have executed these Joint Escrow Instructions as of the day and year first above written.

Very truly yours,

COMPANY:

Fulcrum Therapeutics, Inc.

By: _____
Name: _____
Title: _____

HOLDER:

By: _____
Name: _____

Address: [_____]
[_____]

ESCROW AGENT:

By: _____
Name: _____
Title: Secretary

SIGNATURE PAGE TO JOINT ESCROW INSTRUCTIONS

EXHIBIT B
STOCK ASSIGNMENT SEPARATE FROM CERTIFICATE

STOCK ASSIGNMENT SEPARATE FROM CERTIFICATE

FOR VALUE RECEIVED, I hereby sell, assign and transfer unto () shares of Common Stock, \$0.001 par value per share, of Fulcrum Therapeutics, Inc. (the “**Corporation**”) standing in my name on the books of the Corporation represented by Certificate(s) Number herewith, and do hereby irrevocably constitute and appoint Wilmer Cutler Pickering Hale and Dorr LLP attorney to transfer the said stock on the books of the Corporation with full power of substitution in the premises.

Dated: _____

PARTICIPANT:

[Name]

Name of Spouse (if any):

Instructions to Participant: Please do not fill in any blanks other than the signature line(s). The purpose of the Stock Assignment Separate from Certificate is to enable the Company to acquire the Shares upon exercise of its Right of First Refusal and/or Purchase Option without requiring additional signatures on the part of the Participant or Participant’s spouse, if any. The signature(s) to this assignment must correspond with the name as written upon the face of the certificate, in every particular, without alteration, enlargement, or any change whatever.

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) would likely cause competitive harm to the Company, if publicly disclosed. Double asterisks denote omissions.

RIGHT OF REFERENCE AND LICENSE AGREEMENT

THIS RIGHT OF REFERENCE AND LICENSE AGREEMENT (this "Agreement"), dated as of February 8, 2019 (the "Effective Date"), is made and entered into by and between GlaxoSmithKline Intellectual Property (No. 2) Limited, a company organized under the laws of England and Wales and having a place of business at 980 Great West Road, Brentford, Middlesex TW8 9GS England ("GIP2"), GlaxoSmithKline LLC, a Delaware limited liability company having a place of business at 1250 S. Collegeville Road, Collegeville, PA 19426-0989 ("GSK LLC") and Glaxo Group Limited, a company organized under the laws of England and Wales and having a place of business at 980 Great West Road, Brentford, Middlesex TW8 9GS England ("GGL") (GIP2, GSK LLC and GGL are collectively referred to herein as "GSK"), and Fulcrum Therapeutics, Inc., a Delaware corporation having a place of business at 26 Landsdowne Street, Cambridge, MA 02139 ("Fulcrum"). GSK and Fulcrum may be referred to herein individually as a "Party" and collectively as the "Parties".

RECITALS

WHEREAS, GSK (or its Affiliate) is the owner of the Losmapimod IND and the GSK Intellectual Property (each as defined below);

WHEREAS, Fulcrum desires to obtain a right of reference to the Losmapimod IND and an exclusive license under the GSK Intellectual Property; and

WHEREAS, GSK desires to grant to Fulcrum such rights in accordance with the terms and conditions of this Agreement and the Equity Documents (defined below), which will be executed simultaneously with this Agreement.

NOW THEREFORE, in consideration of the premises and mutual covenants herein contained, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties agree as follows:

ARTICLE I DEFINITIONS

Section 1.1. Definitions.

The following terms, as used herein, have the following meanings:

"Affiliate" means any Person that directly or indirectly, whether *de jure* or *de facto*, is controlled by, controlling or under common control with, a Party, but only for so long as such control shall continue. For purposes of this definition, "control" (including, with correlative meanings, "controlled by", "controlling" and "under common control with") means, with respect

to a Person, possession, direct or indirect, of (a) the power to direct or cause direction of the management and policies of such Person (whether through ownership of securities or partnership or other ownership interests, by contract or otherwise), or (b) at least 50% of the voting securities (whether directly or pursuant to any vested and exercisable option, warrant or other similar arrangement) or other comparable equity interests of such Person. A Person shall cease to be an "Affiliate" under this Agreement upon the date that such Person no longer satisfies the requirements set forth in this definition.

"Business Day" means any day except Saturday, Sunday or any day on which banks are generally not open for business in New York, NY United States or London, England, but in any event excluding the nine (9) consecutive calendar days beginning on December 24th and continuing through and including January 1st of each Calendar Year during the Term.

"Calendar Quarter" means each of the consecutive three (3) month periods ending on March 31, June 30, September 30 and December 31 of any Calendar Year.

"Calendar Year" means each twelve (12) month period commencing on January 1 and ending on December 31.

"Commercially Reasonable Efforts" means, with respect to Fulcrum's obligations under this Agreement, the carrying out of such obligations or tasks with a level of efforts and resources consistent with the commercially reasonable practices of a company of similar size and resources in the biopharmaceutical industry for the research, development or commercialization of a pharmaceutical product of commercial potential comparable to that of the applicable Licensed Product at a similar stage of development or commercialization, taking into account efficacy, safety, patent and regulatory exclusivity, anticipated or approved labeling, present and future market potential, competitive market conditions, costs and risks of development and commercialization, relevant scientific and technical considerations and the profitability of the applicable Licensed Product in light of pricing and reimbursement issues; provided, that Fulcrum shall not take into consideration any amounts owed to GSK under this Agreement. Commercially Reasonable Efforts shall be determined on a market-by-market and Licensed Product-by-Licensed Product basis, and it is anticipated that the level of efforts required shall be different for different markets and Licensed Products and shall change over time, reflecting changes in the status of the Licensed Product and markets involved.

"Compound" means the small molecule p38 inhibitor known as Losmapimod, which molecule is identified on Schedule 1.1 of this Agreement, attached hereto and incorporated herein.

"Control" means, with respect to any item of Data, Patents or other proprietary right, the possession of the right, whether directly or indirectly, and whether by ownership, license, or other right (other than pursuant to this Agreement), to grant an exclusive license under such Data, Patents or other proprietary right.

"Data" means, with respect to the Compound, (i) the documents and data stored on an encrypted hard drive transferred to Fulcrum by GSK prior to the Effective Date and identified

within GSK as “FT04Feb2019” and (ii) the documents, data and information required to be delivered pursuant to [Section 2.5\(b\)](#).

“[Debarred](#)” or “[Debarment](#)” means, with respect to a Person, that such Person (a) is debarred by the FDA pursuant to Section 306 of the United States Federal Food, Drug and Cosmetic Act, or is the subject of conviction described in such section (or is subject to a similar sanction of any other applicable Regulatory Authority), (b) is the subject of an FDA debarment investigation or proceeding (or similar proceeding of any other applicable Regulatory Authority), or (c) has been charged with or convicted under U.S. Law for conduct relating to the development or approval, or otherwise relating to the regulation, of any product under the Generic Drug Enforcement Act of 1992.

“[EMA](#)” means the European Medicines Agency and any successor entity.

“[Equity Documents](#)” has the meaning set forth in [Section 3.1](#) of this Agreement.

“[Exploit](#)” means to research, develop, design, make, use, sell, offer for sale, license, lease, supply, distribute, provide, perform, practice, import, export or otherwise make available, commercialize or exploit any technology, or to allow any Person to do any of the foregoing.

“[EU](#)” means the economic, scientific and political organization of member states known as the European Union, as its membership may be altered from time to time, and any successor thereto. Notwithstanding the foregoing, the EU shall be deemed to include the United Kingdom for purposes of this definition regardless of whether or not the United Kingdom is a member state of the European Union.

“[FDA](#)” means the United States Food and Drug Administration and any successor agency thereto.

“[Field](#)” means all therapeutic uses in humans.

“[First Commercial Sale](#)” means, with respect to a Licensed Product in a particular country, the first sale of such Licensed Product by a Selling Party to a Third Party for end use or consumption in such country.

“[FSHD](#)” means facioscapulohumeral muscular dystrophy.

“[Generic Version](#)” means a product that is (i) approved for the same indication as a Licensed Product and contains the Compound; and (ii) sold by a Third Party that is not a Sublicensee of Fulcrum, under a Regulatory Approval granted to a Third Party.

“[GSK Intellectual Property](#)” means the GSK Patents and the Data.

“[GSK Patents](#)” means the Patents listed on [Schedule 1.2](#) attached hereto and incorporated herein, and all counterpart Patents thereof, and all corresponding Patents throughout the world.

“[IND](#)” means an investigational new drug application filed with the FDA.

“Indemnified Party” has the meaning set forth in Section 8.3(a).

“Law” means any federal, state, local, national or supra-national law (both common and statutory law and civil and criminal law), treaty, convention, rule, directive, legislation, ordinance, regulatory code (including, without limitation, statutory instruments, guidance notes, circulars, directives, decisions, rules and regulations) or similar provision having the force of law or an order of any Regulatory Authority or any self-regulatory organization.

“Licensed Product” means any pharmaceutical preparation that contains the Compound as an active pharmaceutical ingredient, in any and all forms, presentations, delivery systems, dosages and formulations.

“Losmapimod IND” means IND No. [***], previously filed with FDA by GSK or its Affiliates for the Compound, and all amendments of any of the foregoing.

“Marketing Authorization Application” means: (a) in the United States, a New Drug Application (as defined in Title 21, Section 314.50 et seq. of the U.S. Code of Federal Regulations or any successor regulations), including any amendment or supplement thereto, and (b) in any other country or regulatory jurisdiction, an application for Regulatory Approval required for marketing or sale of a Licensed Product in such country or regulatory jurisdiction, including any amendment or supplement thereto.

“Net Sales” means the gross amounts billed or invoiced by Fulcrum, its Affiliates and Sublicensees (each, a “Selling Party”) to any Third Party that is not a Sublicensee with respect to sales of Licensed Products in the Territory, less the following:

- (a) discounts, credits, refunds, wholesaler allowances, inventory management fees and rebates actually allowed by Fulcrum, its Affiliates or Sublicensees with respect to Licensed Products;
- (b) sales, import, export, customs, and value added taxes, and duties directly imposed on the Licensed Products and actually paid by Fulcrum, its Affiliates or Sublicensees, excluding taxes on the net income of Fulcrum, its Affiliates and Sublicensees;
- (c) outbound freight, postage, duties, transportation, handling and insurance costs actually paid by Fulcrum, its Affiliates or Sublicensees with respect to Licensed Products;
- (d) billed or invoiced amounts written off as uncollectible by Fulcrum, its Affiliates or Sublicensees with respect to Licensed Products, provided that if any such written off amount is thereafter collected, such amount shall be included in Net Sales in the Calendar Quarter in which it is collected;
- (e) annual fees due under Section 9008 of the United States Patient Protection and Affordable Care Act of 2010 (Pub. L. No. 111-48) allocable to sales of Licensed Product; and

(f) amounts actually allowed or credited on returns of sales of Licensed Products by Fulcrum, its Affiliates or their Sublicensees.

In no event shall any particular amount identified above be deducted more than once in calculating Net Sales (*i.e.*, no “double counting” of deductions). All discounts, allowances, credits, rebates, and other deductions shall be fairly and equitably allocated to the Licensed Product and other product(s) of Fulcrum, and of its Affiliates and Sublicensees, such that the Licensed Products do not bear a disproportionate portion of such deductions.

Such amounts shall be determined in accordance with either (i) U.S. Generally Accepted Accounting Principles (“GAAP”) or (ii) International Financial Reporting Standards (“IFRS”) depending on the accounting standard used by the applicable Selling Party in such Selling Party’s financial reporting, case consistently applied.

“Patent” means all: (a) letters patent (including inventor’s certificates), including any substitution, extension, registration, confirmation, validation, reissue, re-examination, supplementary protection certificates, confirmation patents, patent of additions, renewal or any like filing thereof; (b) pending applications for letters patent (including applications for inventor’s certificates), including any continuation, division or continuation-in-part thereof and any provisional applications; and (c) any United States and international counterparts to any of (a) and (b) above.

“Person” means an individual, corporation, partnership, limited liability company, association, trust or other entity or organization, including a government or political subdivision or an agency or instrumentality thereof.

“Phase 1 Clinical Trial” means a study of a Licensed Product in healthy individuals or patients, the principal purpose of which is a preliminary determination of safety, tolerability, pharmacological activity or pharmacokinetics, as further defined in 21 C.F.R. 312.21(a), or the corresponding regulations in any jurisdiction or country other than the United States, or any amended or successor regulations, to permit the design of further clinical trials.

“Phase 2 Clinical Trial” means a study of a Licensed Product in the Field in human patients designed or intended to determine initial efficacy, pharmacological effect or dose range or regimen, as further defined in 21 C.F.R. 312.21(b), or the corresponding regulations in any jurisdiction or country other than the United States, or any amended or successor regulations, to permit the design of further clinical trials.

“Phase 3 Clinical Trial” means a pivotal study in the Field in human patients with a defined dose or a set of defined doses of a Licensed Product designed or intended to ascertain efficacy and safety of such Licensed Product for the purpose of enabling the preparation and submission of a Marketing Authorization Application to the competent Regulatory Authority in a country of the Territory, as further defined in 21 C.F.R. 312.21(c), or the corresponding regulations in any jurisdiction or country other than the United States, or any amended or successor regulations.

“Regulatory Approval” means any and all approvals (including supplements, amendments, and pre- and post-approvals), licenses, registrations or authorizations (or waivers) of any national, supra-national (e.g., the European Commission or the Council of the EU), regional, state or local regulatory agency, department, bureau, commission, council or other governmental entity, that are necessary for the manufacture, distribution, use, import, transport, promotion, marketing, offer for sale or sale of a product in a regulatory jurisdiction; but excluding any pricing and reimbursement approval.

“Regulatory Authority” means the applicable national (e.g., the FDA), supra-national (e.g., the European Commission or the Council of the EU), regional, state or local regulatory agency, department, bureau, commission, council or other governmental authority that, in each case, regulates or governs the Exploitation of the Compound or Licensed Product or the granting of Regulatory Approval of a Licensed Product in a regulatory jurisdiction.

“Regulatory Exclusivity” means any exclusive marketing rights or data exclusivity rights granted by a Regulatory Authority (other than Patents) with respect to a Licensed Product sold in a given country, including orphan drug exclusivity, new chemical entity exclusivity, data exclusivity or pediatric exclusivity, which confers an exclusive commercialization period during which Fulcrum or its Affiliates or Sublicensees have the exclusive right to market and sell a Licensed Product in such country.

“Senior Management Designees” has the meaning set forth in Section 10.4(b) of this Agreement.

“Service Provider” means a contract research organization, a contract manufacturing organization or other similar service provider that provides drug development services to Fulcrum.

“Spreadsheet” has the meaning set forth in Section 2.5(b) of this Agreement.

“Sublicensee” means a Third Party that has been granted a sublicense under the rights granted to Fulcrum pursuant to Section 2.3 of this Agreement.

“Supplemental Data” has the meaning set forth in Section 2.5(c) of this Agreement.

“Term” has the meaning set forth in Section 9.1 of this Agreement.

“Territory” means worldwide.

“Third Party” means any Person other than GSK or Fulcrum or any of their respective Affiliates.

“Third Party Claim” means any, action, suit, proceeding, liability or obligation brought by a Third Party.

ARTICLE II
LICENSE GRANT; DATA TRANSFER

Section 2.1. Right of Reference.

GSK hereby grants Fulcrum a right of reference as to the Losmapimod IND. Within [**] following the Effective Date GSK shall deliver, or shall cause to be delivered, to Fulcrum an executed Letter of Authorization (in the form of Exhibit A) to the FDA confirming that Fulcrum, its Affiliates and its Sublicensees have the right to reference the Losmapimod IND in connection with their Exploitation of the Compound and Licensed Products as provided under this Agreement.

Section 2.2. License Grant.

Subject to the terms and conditions of this Agreement, GSK, on behalf of itself and its Affiliates, shall and hereby does, effective as of the Effective Date, grant Fulcrum an exclusive (subject to Section 2.4), royalty-bearing, sublicensable (subject to Article IV) license under the GSK Intellectual Property to Exploit the Compound and Licensed Products in the Field in the Territory.

Section 2.3. Sublicenses.

(a) Subject to Sections 2.3(b) and 4.1, Fulcrum may sublicense the rights granted to it by GSK under Section 2.2. Each sublicense to a Sublicensee must be granted pursuant to a written sublicense agreement consistent with the requirements of this Agreement applicable thereto, and Fulcrum shall provide to GSK, within [**] after the execution of such sublicense agreement, a complete copy thereof, which copy Fulcrum may redact for financial terms and other information not required to evidence Fulcrum's compliance with the sublicensing terms of this Agreement.

(b) Commencing on the Effective Date and continuing until the date on which Fulcrum first submits an IND to the FDA for a Licensed Product, Fulcrum shall not sublicense any of the rights as to Licensed Products in the United States granted to Fulcrum by GSK under Section 2.2 to any Third Party without GSK's prior written consent; *provided, however*, that the terms of this Section 2.3(b) shall not apply to any sublicense by Fulcrum to any Service Provider.

(c) Fulcrum shall remain responsible for its obligations, including as set forth in Sections 3.2, 3.3 and 3.4, that have been delegated, subcontracted or sublicensed to any of its Affiliates or Sublicensees, and Fulcrum shall be liable for any failure by any Affiliate or Sublicensee of Fulcrum to comply with the terms of this Agreement to the extent that compliance with such terms has been delegated, subcontracted or sublicensed to such Affiliate or Sublicensee.

Section 2.4. Rights Retained by GSK.

Fulcrum shall receive only those rights of GSK expressly granted by GSK under the provisions of this Agreement, and any right of GSK not expressly granted to Fulcrum under the provisions of this Agreement shall be retained by GSK. For the avoidance of doubt, (a) GSK

and its Affiliates shall retain the right, without the right to grant sublicenses, to conduct nonclinical research under the GSK Intellectual Property; and (b) with Fulcrum's consent (as described below), GSK's [**] may, under the GSK Patents, [**] solely relating to the use of Licensed Product in connection with the [**]; *provided, however*, that, (i) prior to [**], GSK shall seek Fulcrum's consent thereto and, in connection therewith, shall [**] to Fulcrum for its review, and (ii) Fulcrum shall determine whether to grant such consent based on such protocol and all other relevant factors, which consent Fulcrum shall not unreasonably withhold or delay. This Agreement creates no obligation for GSK or any of its Affiliates to remove or segregate the Data from its systems for any purpose.

Section 2.5. Data Transfer.

(a) To the extent not already provided prior to the Effective Date, within [**] following the Effective Date, GSK shall cooperate with Fulcrum's reasonable instructions to effect the transfer of electronic copies of the Data to Fulcrum (the "Data Transfer").

(b) Commencing on the Effective Date, GSK shall use commercially reasonable efforts to deliver to Fulcrum (i) those SAS datasets related to the Compound, which are set forth on Schedule 2.5(b), within [**] following the Effective Date, and (ii) as requested by Fulcrum in a spreadsheet named "GSK Information Requests_vMaster 05 Feb (version 2) sent to GSK on February 5, 2019 by [**] of Fulcrum to [**] of GSK (the "Spreadsheet")": (A) the drug substance and placebo batch records related to the physical material of the Compound being transferred to Fulcrum as described in Section 2.6 below, which are set forth in request number [**] and request numbers [**] (inclusive) of the Spreadsheet, within [**] following the Effective Date and (B) the Microsoft Word and PDF files for all nonclinical and clinical study reports related to the Compound, which are set forth in request numbers [**] (inclusive) of the Spreadsheet, within [**] following the Effective Date to the extent not previously delivered by GSK to Fulcrum. If, upon expiration of the applicable timeframes in this Section 2.5(b), GSK has not delivered all Data described in this Section 2.5(b) then GSK and Fulcrum shall use good faith efforts to implement an appropriate alternative means to provide Fulcrum with any such Data that GSK has not delivered within the applicable timeframes in this Section 2.5(b), to the extent such Data is available.

(c) For a period of [**] commencing on the Effective Date, Fulcrum may request, and GSK shall use commercially reasonable efforts to provide, any Data not provided in the initial Data Transfer. During such [**] period commencing on the Effective Date, Fulcrum may also request that GSK provide information that is not Data that is reasonably related to the Compound and may be useful to Fulcrum for further development of, or the submission of regulatory filings relating to, the Compound for the treatment of FSHD (such information, "Supplemental Data"), to the extent such Supplemental Data is in GSK's (or its Affiliates') possession and is Controlled by GSK (or its Affiliates), and GSK shall use commercially reasonable efforts to locate or provide any such requested Supplemental Data. Any Supplemental Data that may be provided by GSK to Fulcrum as provided herein shall be deemed to be Data.

Section 2.6. Material Transfer.

GSK shall provide to Fulcrum the physical material of the Compound, including clinical placebo tablets, which are set forth on Schedule 2.6 attached hereto and incorporated herein, and which physical transfer GSK shall initiate within [**] of the Effective Date with respect to all physical material of the Compound set forth on Schedule 2.6.

Section 2.7. Reports.

Within [**] after then end of each Calendar Year during the Term, Fulcrum shall provide a written report to GSK, which report shall summarize in reasonable detail all of the development, regulatory and commercialization activities conducted by or on behalf of Fulcrum or its Affiliates with respect to the Compound and Product in the Territory.

**ARTICLE III
EQUITY ISSUANCE; PAYMENTS**

Section 3.1. Equity Issuance.

(a) Issuance of Equity. In partial consideration for the licenses and other rights granted to Fulcrum hereunder, Fulcrum shall issue to GSK twelve million five hundred thousand (12,500,000) shares of Fulcrum's Series B Preferred Stock pursuant to a subscription agreement and any other agreements by and between GSK and Fulcrum and dated as of the date hereof, relating to the issuance of such shares and any other rights related thereto to GSK (collectively, the "Equity Agreements").

(b) Equity Agreements. As a condition precedent to the effectiveness of this Agreement, the Parties shall have duly authorized, executed and delivered the all of the Equity Agreements and performed their respective obligations that are required to be performed thereunder.

Section 3.2. Development and Regulatory Milestone Payments.

Fulcrum shall make each of the development and regulatory milestone payments set forth in the table below in this Section 3.2 to GSK within [**] after the first achievement (whether by or on behalf of Fulcrum or any of its Affiliates or, subject to Section 2.3, Sublicensees) of the corresponding milestone event set forth in the table below in this Section 3.2 by the first Licensed Product to achieve such a milestone event. Fulcrum shall notify GSK within [**] of the achievement of each development and regulatory milestone event. Each milestone payment set forth in the table below in this Section 3.2 shall be paid only once during the Term, for the first time any Licensed Product reaches such milestone event during the Term, and regardless of the number of Licensed Products that achieve such milestone event, the number of times such milestone event is achieved by any Licensed Product, or the number of additional Licensed Products that subsequently achieve any such milestone event. Notwithstanding the foregoing, in the event any regulatory milestone event in (c) through (e) is achieved, prior to the achievement of a development milestone in (a) or (b) (the "skipped milestone"), the applicable skipped

milestone will become due and payable together with the applicable regulatory milestone in (c), (d) or (e). For clarification, the total milestone payments that may become payable under this Section 3.2 if all milestone events in the table below in this Section 3.2 are achieved is thirty-seven million five hundred thousand dollars (\$37,500,000).

Milestone Event	Milestone Payment
(a) Initiation of the first Phase 2 Clinical Trial for a Licensed Product	\$ 2,500,000
(b) [**]	[**]
(c) [**]	[**]
(d) [**]	[**]
(e) [**]	[**]

Section 3.3. Sales Milestone Payments.

Fulcrum shall make each of the following one-time sales milestone payments to GSK within [**] after the end of the Calendar Quarter in which aggregate annual Net Sales of the first Licensed Product in the Territory to reach the threshold(s) specified in the table below in this Section 3.3. Fulcrum shall notify GSK promptly of the achievement of each such sales threshold. If more than one sales threshold is reached in any given Calendar Year, then the applicable milestone payment for each such achievement shall be due and owing with respect to such Calendar Year. Each milestone payment set forth in the table below in this Section 3.3 shall be paid only once during the Term, for the first time any Licensed Product reaches such sales milestone threshold, and regardless of the number of Licensed Products that achieve such sales milestone threshold, the number of times such milestone event is achieved by any Licensed Product, or the number of additional Licensed Products for which such milestone event is subsequently achieved. For clarification, the total milestone payments that may become payable under this Section 3.3 if all sales milestone thresholds in the table below in this Section 3.3 are achieved is sixty million dollars (\$60,000,000).

Threshold for Aggregate Annual Worldwide Net Sales	Milestone Payment
[**]	[**]
[**]	[**]
[**]	[**]

Section 3.4. Royalty Payments.

(a) Royalty Rates. Fulcrum shall pay to GSK tiered royalties on the aggregate annual Net Sales of Licensed Products sold in the Territory during each Calendar Year quarterly within [**] after the end of such Calendar Quarter during the Royalty Term at the applicable rate(s) set forth below with such royalties to be calculated by multiplying the applicable incremental amount of Net Sales of such Licensed Products in the Territory in such Calendar Quarter by the corresponding royalty rate set forth in the table below and by subsequently making the applicable adjustments in accordance with Section 3.4(c).

Annual Net Sales of Licensed Product	Royalty Rate
For that portion of annual Net Sales less than or equal to \$[**]	[**]%
For that portion of annual Net Sales greater than \$[**] and less than or equal to \$[**]	[**]%
For that portion of annual Net Sales greater than \$[**]	[**]%

(b) Royalty Term. Royalties under this Section 3.4 shall be payable on a country-by-country basis in the Territory during the period commencing on the First Commercial Sale of such Licensed Product in such country and continuing on until the earlier of (i) approval of a Generic Version of such Licensed Product by the applicable Regulatory Agency on a country-by-country basis; and (ii) the tenth (10th) anniversary of the First Commercial Sale of such Licensed Product in such country (the "Royalty Term"). Upon expiration of the Royalty Term for any Licensed Product in a given country, the licenses granted to Fulcrum under Section 2.2 with respect to such Licensed Product in such country shall automatically become fully paid-up, perpetual and royalty-free and shall survive any expiration or termination of this Agreement, and Net Sales of such Licensed Product in such country shall thereafter be excluded from aggregate annual Net Sales of such Licensed Product for purposes of calculating royalties pursuant to Section 3.4(a).

(c) Royalty Adjustments.

(i) During any applicable Royalty Term, following the expiration of Regulatory Exclusivity for any Licensed Product on a country-by-country basis, the royalty rates in Table 3.4(a) applicable to Net Sales of such Licensed Products in such country will be reduced by [**] percent ([**]%).

(ii) If Fulcrum or any of its Affiliates or Sublicensees, as applicable, determines, in its reasonable judgment, that it is necessary to obtain a license from any Third Party (each a "Third Party License") under any Patents in order to Exploit a Licensed Product in a country, then Fulcrum may deduct [**] percent ([**]%) of any license fees under such Third Party License payable by Fulcrum or any Affiliate or

Sublicensee in any Calendar Quarter to such Third Party with respect to sales of such Licensed Product in such country under such Third Party License from the royalty payment that would otherwise be due with respect to Net Sales of such Licensed Product in such country in such Calendar Quarter pursuant to Section 3.4(a) (as adjusted by Section 3.4(c)(i), as applicable); *provided, however*, that in no event shall any royalty payment to GSK on Net Sales of any Licensed Product in any country in any Calendar Quarter be reduced to less than **[**]** percent (**[**]**%) of the royalties that would otherwise be owed to GSK with respect to Net Sales of such Licensed Product under Section 3.4(a) (as adjusted by Section 3.4(c)(i), if applicable). Any amount of royalties paid to such Third Party which is entitled to be deducted under this Section 3.4(c)(ii) but is not deducted as a result of the foregoing limitation shall be carried over and applied against royalties payable to GSK in respect of such Licensed Product in such country in subsequent Calendar Quarters until the full deduction is taken.

Section 3.5. Reports; Audits.

(a) Until the expiration of the Term as to all Licensed Products in all countries, Fulcrum agrees to make written reports to GSK within **[**]** after the end of each Calendar Quarter covering sales by Fulcrum, its Affiliates and Sublicensees of any Licensed Product that is subject to Fulcrum's royalty obligations hereunder on a country-by-country basis during such Calendar Quarter. Each such written report shall provide (a) the Net Sales during such Calendar Quarter, in US dollars, (b) the royalties payable, in US dollars, which accrued hereunder with respect to such Net Sales and (c) the exchange rate used in calculating any of the foregoing. The information contained in each report under this Section 3.5 shall be considered Confidential Information of Fulcrum and its Affiliates.

(b) Fulcrum agrees, upon not less than **[**]** prior written notice, to permit, and to require its Affiliates and Sublicensees to permit, an independent accounting firm selected by GSK and reasonably acceptable to Fulcrum to examine the books and records relating to any Licensed Product for the purpose of verifying reports provided by Fulcrum under Section 3.5(a). Such audit shall not (i) be performed more frequently than **[**]** period (unless a previous audit during such **[**]** period revealed a material discrepancy with respect to such period), or (ii) be repeated for any Calendar Quarter, and shall be conducted for the sole purpose of verifying the accuracy and completeness of all financial, accounting and numerical information and calculations provided under this Agreement. The independent accounting firm shall have the right to make copies of relevant portions of Fulcrum's books and records; *provided* that any such copies shall be the Confidential Information of Fulcrum, shall be protected by appropriate confidentiality obligations and shall not be shared with GSK or any other Person. The independent accounting firm will prepare and provide to the Parties a written report stating only whether the reports submitted, and amounts paid hereunder were correct or incorrect, and the amounts of any discrepancies. GSK shall bear the cost of any audit conducted under this Section 3.5(b) unless a discrepancy greater than **[**]** percent (**[**]**%) over any Calendar Year is found, in which case Fulcrum shall bear the cost of such audit.

Section 3.6. Payment Method.

All Royalty Payments shall be made in US dollars in immediately available funds via either a bank wire transfer, an ACH (automated clearing house) mechanism, or any other means of electronic funds transfer, at Fulcrum's election, to a bank account specified by GSK in a notice at least [**] before the payment is due.

Section 3.7. Late Payments.

If Fulcrum shall fail to make a timely Royalty Payment pursuant to the terms of this Agreement, GSK shall provide written notice of such failure to Fulcrum (a "Late Payment Notice"), and interest shall accrue on the past due amount starting on the date of the Late Payment Notice at the prime or equivalent rate per annum quoted by the Wall Street Journal, Eastern Edition on the first Business Day after such payment is due, plus [**] percent ([**]%), computed for the actual number of days after the date of the Late Payment Notice that the payment was past due.

**ARTICLE IV
RIGHT OF FIRST NEGOTIATION**

Section 4.1. Negotiation Right.

Commencing on the Effective Date and until the completion of a Phase 2 Clinical Trial for a Licensed Product, if Fulcrum wishes to sublicense to any Third Party any of the rights granted to Fulcrum by GSK under Section 2.2 in any country(ies) in the Territory other than the United States, Fulcrum shall, prior to entering into a sublicense agreement with any Third Party, notify GSK in writing of Fulcrum's desire to sublicense its rights to a Third Party and the terms on which Fulcrum proposes to grant such sublicense; *provided, however*, that the terms of this Section 4.1 shall not apply to any sublicense to any Service Provider. GSK shall have [**] from receipt of such notice to decide whether to enter into further negotiations with Fulcrum for GSK or its Affiliate to Exploit Licensed Product in the applicable country(ies) in the Territory other than the United States. If GSK does not elect for it or its Affiliate to Exploit Licensed Product in the applicable country(ies) in the Territory other than the United States or does not respond to Fulcrum's notice within such [**] period, subject to Section 2.3, Fulcrum may sublicense the rights granted to Fulcrum by GSK under Section 2.2 in the applicable country(ies) in the Territory other than the United States to any Third Party, subject to Section 2.3. If GSK elects within such [**] period to negotiate for it or its Affiliate to Exploit Licensed Product in the applicable country(ies) in the Territory other than the United States, then the Parties shall negotiate in good faith for a period of not more than [**] after such election by GSK. If the Parties have not reached an agreement within such [**] period, then Fulcrum shall have the right to (i) enter into negotiations with any Third Party for the sublicense of its rights granted to Fulcrum by GSK under Section 2.2 in the applicable country(ies) in the Territory other than the United States and (ii) grant sublicenses in the applicable country(ies) in the Territory without further obligations to negotiate with GSK, provided that any such sublicense (x) is subject to Section 2.3 and (y) does not include terms that are in the aggregate less favorable than those offered by GSK. For the avoidance of doubt, GSK's right of first negotiation under this Section 4.1 shall expire upon the first completion of a Phase 2 Clinical Trial for a Licensed Product.

ARTICLE V
INTELLECTUAL PROPERTY

Section 5.1. Patent Maintenance.

(a) GSK Patents. All decisions and actions with respect to the maintenance of the GSK Patents shall be the responsibility of Fulcrum, at Fulcrum's sole cost and expense. Fulcrum may abandon or discontinue the maintenance of any GSK Patent in a country; *provided* that Fulcrum first notifies GSK in writing at least [**] in advance of the due date of any payment or other action that is required to maintain such GSK Patent, and, upon such notice, GSK shall have the option, but not the obligation, to maintain such GSK Patent in the Territory at its sole cost and expense.

(b) Patent Term Extensions. As between the Parties, Fulcrum shall have the sole right, but not the obligation, at its sole cost and expense, to file for and seek to obtain patent term extensions (including any pediatric exclusivity extensions as may be available) or supplemental protection certificates or their equivalents in any country with respect to the GSK Patents based on Regulatory Approvals for the GSK Patents.

(c) Data Exclusivity. With respect to data exclusivity periods, Fulcrum shall have the sole right, but not the obligation, at its sole cost and expense, to seek, maintain and enforce all such data exclusivity periods available for Licensed Products.

Section 5.2. Patent Enforcement.

(a) Notification. If either Party becomes aware of any existing or threatened infringement of any GSK Patent in the Field in the Territory, including (i) any such existing or threatened infringement on account of a Third Party's Exploitation of the Compound or any Generic Version of a Licensed Product in the Field in any country in the Territory, or (ii) any certification filed by a Third Party in the United States pursuant to the Drug Price Competition and Patent Term Restoration Act of 1984 (or any successor legislation) or similar provisions in other jurisdictions, in connection with an abbreviated new drug application or a paper new drug application (or equivalent) with respect to the Compound or any Licensed Product in the Field in any country in the Territory, or any other similar Third Party communication, including notices pursuant to §§ 101 and 103 of such act from any person or entity who has filed an abbreviated new drug application or a paper new drug application (or equivalent) with respect to the Compound or any Generic Version of a Licensed Product in the Field ((i) and (ii), collectively, "Competitive Infringement"), it shall promptly notify the other Party in writing to that effect, and the Parties will consult with each other regarding any actions to be taken with respect to such Competitive Infringement.

(b) Right to Enforce. Fulcrum shall have the first right, but shall not be obligated, to bring and control an infringement action with respect to any Competitive Infringement of any GSK Patent, at Fulcrum's sole cost and expense. If Fulcrum does not bring such an action with respect to a GSK Patent (or settle or otherwise secure the abatement of such infringement) prior to the earlier of: (i) [**] following GSK's receipt or delivery of the notice under Section 5.2(a), or (ii) [**] before the deadline, if any, set forth in the applicable Laws for the filing of such

actions, GSK shall have the right, but not the obligation, to bring and control any such action, at its own expense and by counsel of its own choice.

(c) **Cooperation.** Each Party shall cooperate fully with the enforcing Party in such enforcement, at such enforcing Party's request and expense, including joining such action as a party plaintiff if required by applicable Laws to pursue such action. The enforcing Party shall keep the other Party regularly informed of the status and progress of such enforcement efforts and shall reasonably consider the other Party's comments on any such efforts. The non-enforcing Party shall be entitled to separate representation in such matter by counsel of its own choice and at its own expense, but such Party shall at all times cooperate fully with the enforcing Party. Neither Party shall have the right to settle any patent infringement litigation under this Section 5.2 in a manner that diminishes the rights or interests of the other Party without the prior written consent of such other Party, such consent not to be unreasonably withheld, conditioned or delayed.

(d) **Expenses and Recoveries.** The enforcing Party bringing a claim, suit or action under this Section 5.2 shall be solely responsible for any expenses incurred by such Party as a result of such claim, suit or action. If such Party recovers monetary damages in such claim, suit or action, except as otherwise agreed by the Parties in connection with a cost-sharing arrangement, such recovery shall be allocated first to the reimbursement of any expenses incurred by the Parties in such litigation, and any remaining amounts shall be shared as follows: the remaining amount of any such recovery shall be deemed Net Sales for the Calendar Quarter in which such recovery payment is received by the Parties, and GSK shall receive royalty payments on such amounts as set forth in Section 3.4.

ARTICLE VI
REPRESENTATIONS AND WARRANTIES; GSK COVENANTS

Section 6.1. Representations and Warranties of Both Parties.

Each Party hereby represents and warrants to the other Party, as of the Effective Date, that:

- (a) Such Party is duly organized, validly existing and in good standing under the Laws of the jurisdiction of its incorporation and has full corporate power and authority to enter into this Agreement and to carry out the provisions hereof;
- (b) Such Party has taken all necessary action on its part to authorize the execution and delivery of this Agreement and the performance of its obligations hereunder;
- (c) This Agreement has been duly executed and delivered on behalf of such Party, and constitutes a legal, valid, binding obligation, enforceable against it in accordance with the terms hereof;
- (d) The execution, delivery and performance of this Agreement by such Party does not and will not conflict with any agreement or any provision thereof, or any instrument or understanding, oral or written, to which it is or becomes a party or by which it is or becomes

bound, nor violate any Law or regulation of any court, governmental body or administrative or other agency having jurisdiction over such Party; and

(e) No government authorization, consent, approval, license, exemption of, or filing or registration with any court or governmental department, commission, board, bureau, agency or instrumentality, domestic or foreign, under any Laws currently in effect, is necessary for its execution and delivery of this Agreement.

Section 6.2. Additional Representations and Warranties of GSK.

GSK hereby represents and warrants to Fulcrum, as of the Effective Date, that:

(a) GSK or its Affiliates Control the Losmapimod IND and the GSK Intellectual Property and is entitled to grant the rights and licenses under the Losmapimod IND and the GSK Intellectual Property specified herein; and

(b) GSK has not granted a right of reference to the Losmapimod IND or licensed the GSK Intellectual Property to any Third Party.

Section 6.3. GSK Covenants.

(a) GSK shall not grant to any Third Party any rights that would be inconsistent with Fulcrum's rights hereunder.

(b) GSK shall not assign, transfer, convey or otherwise encumber its right, title and interest in and to the Losmapimod IND or the GSK Intellectual Property in a manner that conflicts with any rights granted to Fulcrum hereunder.

Section 6.4. Fulcrum Covenants. During the Term:

(a) Fulcrum hereby covenants that it and its Affiliates shall use Commercially Reasonable Efforts to develop and commercialize a Licensed Product for FSHD in the Territory.

(b) Fulcrum and its Affiliates shall conduct, and shall use Commercially Reasonable Efforts to cause its Sublicensees and Service Providers to conduct, all activities contemplated under this Agreement in accordance with applicable Law.

(c) Fulcrum and its Affiliates will conduct its business and all activities with respect to the Licensed Product in compliance with the Foreign Corrupt Practices Act of 1977, the UK Bribery Act of 2010 and any other applicable anti-corruption laws.

(d) Neither Fulcrum nor any of its Affiliates will knowingly use in any capacity in connection with the Exploitation of any Licensed Product, any Person who has been Debarred. Fulcrum shall notify GSK immediately upon becoming aware that any Person who is performing services with respect to any Licensed Product has been Debarred or if any claim is pending or, to the best of Fulcrum's knowledge, threatened, relating to the Debarment of Fulcrum, its Affiliates or any Person in connection with the Exploitation of any Licensed Product. For the avoidance of doubt, neither Fulcrum nor any of its Affiliates shall have any liability to GSK or any of its

Affiliates as a result of any Debarred Person's involvement in the Exploitation of any Licensed Product to the extent Fulcrum, having instituted the policies and procedures set forth in Section 6.4(e), had no knowledge of such Person's Debarment or any claim (whether pending or threatened) relating to the Debarment of such Person, provided that Fulcrum takes prompt action to terminate such Debarred Person's involvement in the Exploitation of any Licensed Product upon learning of such Debarment or claim relating to the Debarment of such Person.

(e) Fulcrum and its Affiliates will maintain internal policies and procedures designed to reasonably ensure that neither Fulcrum nor any of its Affiliates will knowingly use in any capacity in connection with the Exploitation of any Licensed Product, any Person who has been Debarred.

Section 6.5. No Other Warranties.

EXCEPT AS OTHERWISE EXPRESSLY SET FORTH IN THIS AGREEMENT, NEITHER PARTY MAKES ANY REPRESENTATION OR WARRANTY OF ANY KIND, EITHER EXPRESS, IMPLIED, STATUTORY OR OTHERWISE, WITH RESPECT TO THE SUBJECT MATTER OF THIS AGREEMENT (INCLUDING, WITHOUT LIMITATION, THE DATA, LOSMAPIMOD IND, COMPOUND, ANY LICENSED PRODUCT OR GSK INTELLECTUAL PROPERTY), INCLUDING ANY WARRANTY OF MERCHANTABILITY, NONINFRINGEMENT, OR FITNESS FOR A PARTICULAR PURPOSE. EACH PARTY DISCLAIMS ANY REPRESENTATION OR WARRANTY THAT THE EXPLOITATION OF LICENSED PRODUCT PURSUANT TO THIS AGREEMENT WILL BE SUCCESSFUL.

**ARTICLE VII
CONFIDENTIALITY**

Section 7.1. Confidentiality.

(a) During the Term and for [**] thereafter, each Party shall maintain Confidential Information (as defined in Section 7.1(b)) of the other Party in confidence, and shall not disclose, divulge or otherwise communicate such Confidential Information to others (except for agents, directors, officers, employees, consultants, subcontractors, Affiliates, advisors, licensees, sublicensees, partners and potential licensees, sublicensees and partners (collectively, "Agents") under obligations of confidentiality at least as restrictive as set forth in this Article VII) or use it for any purpose other than in connection with the Exploitation of the Compound or any Licensed Product pursuant to this Agreement, and each Party shall exercise commercially reasonable efforts to prevent the unauthorized disclosure of such Confidential Information by any of its Agents, which efforts shall be at least as diligent as those generally used by such Party in protecting its own confidential and proprietary information. Each Party will be responsible for a breach of this Section 7.1 by its Agents. For clarity, Fulcrum may disclose Confidential Information of GSK (a) to governmental authorities (i) to the extent desirable to obtain or maintain INDs or regulatory approvals for the Compound or any Licensed Product within the Territory and (ii) in order to respond to inquiries, requests or investigations by governmental authorities; (b) to outside consultants, scientific advisory boards, managed care organizations, and non-clinical and clinical investigators to the extent necessary to Exploit the Compound or

any Licensed Product; (c) to the extent useful to develop, manufacture and commercialize the Compound or any Licensed Product; and (d) to the extent necessary or useful in order to enjoy its rights under this Agreement; *provided* that Fulcrum shall obtain the same confidentiality obligations from any Third Parties to which it discloses the Confidential Information of GSK as it obtains with respect to its own similar types of confidential information.

(b) Confidential Information. “Confidential Information” means all trade secrets or other proprietary information, including any proprietary data and materials (whether or not patentable or protectable as a trade secret), regarding a Party’s or its Affiliate’s or licensor’s technology, products, business, financial status or prospects or objectives regarding the Licensed Products that is disclosed by a Party to the other Party. All information disclosed prior to the Effective Date by a Party to the other Party pursuant to the Mutual Non-Disclosure Agreement by and between the Parties, dated as of June 4, 2018 through the Effective Date (the “Confidentiality Agreement”), shall be deemed “Confidential Information” of such disclosing Party. Notwithstanding the foregoing, there shall be excluded from the foregoing definition of Confidential Information any of the foregoing that:

(i) either before or after the date of the disclosure to the receiving Party is lawfully disclosed to the receiving Party by a Third Party without any violation of any obligation to the other Party; or

(ii) either before or after the date of the disclosure to the receiving Party, becomes published or generally known to the public through no fault or omission on the part of the receiving Party or its Agents; or

(iii) is independently developed by or for the receiving Party without reference to or reliance upon the disclosing Party’s Confidential Information as demonstrated by contemporaneous written records of the receiving Party.

Notwithstanding the foregoing, the receiving Party may disclose the disclosing Party’s Confidential Information if it is required to be disclosed to comply with applicable Laws, to defend or prosecute litigation or to comply with governmental regulations or the regulations or requirements of any stock exchange, *provided* that the receiving Party promptly provides prior notice of such disclosure to the other Party and uses commercially reasonable efforts to avoid or minimize the degree of such disclosure.

(c) Terms of this Agreement. Neither Party may disclose the terms of this Agreement except to the extent required to comply with applicable Laws or legal process, including the rules and regulations of the U.S. Securities and Exchange Commission, or similar agency in any country other than the United States, or of any stock exchange, including Nasdaq. Notwithstanding the foregoing, before disclosing the terms of this Agreement with respect to any filings with the U.S. Securities and Exchange Commission or similar agency in any country other than the United States or of any stock exchange, including Nasdaq, on which securities issued by a Party or a Party’s Affiliate are traded, the Parties will, prior to any such disclosure, agree upon the redaction of certain provisions of this Agreement, and each Party will use commercially reasonable efforts to seek confidential treatment for such terms as may be reasonably requested by the other Party.

(d) **Return of Confidential Information.** Upon the termination of this Agreement (other than on expiration of this Agreement following which Fulcrum's license rights hereunder survive in accordance with Section 9.1), each Party shall return the other Party's Confidential Information or destroy the other Party's Confidential Information at the other Party's request; provided, that each Party may retain one (1) copy of the other Party's Confidential Information for archival purposes only and neither Party shall be required to return or destroy Confidential Information of the other Party stored on automatically created back-up computer systems. Notwithstanding the foregoing, each Party shall continue to be bound by its obligations of confidentiality under this Article VII.

(e) **Publicity.** The Parties agree that following the Effective Date Fulcrum may issue a mutually agreed press release announcing the execution of this Agreement. Any press release or other public announcement relating to the terms of this Agreement will first be reviewed and approved in writing by both Parties, such approval not to be unreasonably withheld; *provided, however*, that any disclosure the minimum information of which is required by applicable Law (including the rules of a securities exchange), as reasonably advised by the disclosing Party's counsel, may be made without the prior consent of the other Party, although the other Party will be given prompt notice of any such legally required disclosure and to the extent practicable will be provided an opportunity to comment on the proposed disclosure and the disclosing Party will consider in good faith any comments provided by the other Party on such proposed disclosure.

ARTICLE VIII INDEMNIFICATION

Section 8.1. Indemnification by GSK.

GSK will defend, indemnify and hold harmless Fulcrum, its Affiliates and its and their respective directors, officers, employees and agents (each a "Fulcrum Indemnitee") from and against any and all Third Party Claims (including without limitation reasonable attorneys' fees and court costs) that constitute, or arise out of or in connection with:

- (a) any misrepresentation or breach of warranty made by GSK under Sections 6.1 and 6.2;
- (b) any default by GSK or its Affiliates in the performance or observance of any of its covenants or agreements hereunder; or
- (c) the negligence or willful misconduct of any of GSK or its Affiliates in connection with GSK's performance of this Agreement;

except, in each case ((a)-(c)) for those Third Party Claims for which Fulcrum, in whole or in part, has an obligation to indemnify GSK pursuant to Section 8.2 hereof, as to which Third Party Claims each Party shall indemnify the other to the extent of their respective Liability for the Third Party Claim.

Section 8.2. Indemnification by Fulcrum.

Fulcrum will defend, indemnify and hold harmless GSK, its Affiliates and its and their respective directors, officers, employees and agents (each a “GSK Indemnitee”) from and against any and all Third Party Claims (including without limitation reasonable attorneys’ fees and court costs) that constitute, or arise out of or in connection with:

- (a) any misrepresentation or breach of warranty made by Fulcrum under Section 6.1;
- (b) any default by Fulcrum, its Affiliates or any Sublicensees in the performance or observance of any of its covenants or agreements hereunder;
- (c) the Exploitation of the Compound or Licensed Products by Fulcrum, its Affiliates or Sublicensees, including all Third Party Claims involving death or bodily injury caused or allegedly caused as a result of the Exploitation of the Compound or Licensed Products by Fulcrum or its Affiliates or its Sublicensees inside the Territory;
- (d) any actual or alleged infringement of any trademark, patent right or other intellectual property right, or misappropriation of any trade secret, of any Third Party as a result of the Exploitation of the Compound or Licensed Products by Fulcrum or its Affiliates or its Sublicensees inside the Territory; or
- (e) the negligence or willful misconduct of any of Fulcrum, its Affiliates or Sublicensees in connection with Fulcrum’s performance of this Agreement;

except, in each case ((a)-(e)) for those Third Party Claims for which GSK, in whole or in part, has an obligation to indemnify Fulcrum pursuant to Section 8.1 hereof, as to which Third Party Claims each Party shall indemnify the other to the extent of their respective Liability for the Third Party Claim.

Section 8.3. Procedure.

(a) A Fulcrum Indemnitee or a GSK Indemnitee seeking indemnification pursuant to this Article VIII (an “Indemnified Party”) shall give prompt written notice to the Party from whom indemnification is sought (the “Indemnifying Party”) of the commencement or assertion of any Third Party Claim for which indemnification may be sought (it being understood and agreed, however, that the failure by an Indemnified Party to give notice of a Third Party Claim as provided in this Section 8.3 shall not relieve the Indemnifying Party of its indemnification obligation under this Agreement except and only to the extent that such Indemnifying Party is actually prejudiced as a result of such failure to give notice).

(b) Within [**] after delivery of such notification, the Indemnifying Party may, upon written notice thereof to the Indemnified Party, assume control of the defense of such Third Party Claim with counsel reasonably satisfactory to the Indemnified Party. If the Indemnifying Party does not assume control of such defense, the Indemnified Party shall control such defense and, without limiting the Indemnifying Party’s indemnification obligations, the Indemnifying Party shall reimburse the Indemnified Party for all costs and expenses, including reasonable attorneys’ fees and disbursements, incurred by the Indemnified Party in defending itself within [**] after receipt of any invoice therefor from the Indemnified Party. The Party not controlling such

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defense may participate therein at its own expense; *provided, however*, that, if the Indemnifying Party assumes control of such defense and the Indemnified Party in good faith concludes, based on written advice from outside counsel, that the Indemnifying Party and the Indemnified Party have conflicting interests with respect to such Third Party Claim sufficiently adverse to make unadvisable the representation by the same counsel of both Parties under Law, ethical rules or equitable principles, the Indemnifying Party shall be responsible for the reasonable fees and expenses of a single counsel to the Indemnified Party in connection therewith. The Party controlling such defense shall keep the other Party advised of the status of such Third Party Claim and the defense thereof and shall consider recommendations made by the other Party with respect thereto.

(c) The Indemnified Party shall not agree to any settlement of such Third Party Claim without the prior written consent of the Indemnifying Party, which consent shall not be unreasonably withheld, delayed or conditioned; *provided, that*, if the Indemnifying Party does not assume the defense of such Third Party Claim in accordance with Section 8.3(b), the Indemnified Party may thereafter agree to a settlement of such Third Party Claim that does not impose obligations on the Indemnifying Party that are more burdensome than the Indemnifying Party’s indemnification obligations under this Agreement. The Indemnifying Party shall not agree to any settlement of such Third Party Claim or consent to any judgment in respect thereof that does not include a complete and unconditional release of the Indemnified Party from all liability with respect thereto, that imposes any liability or obligation on the Indemnified Party or that acknowledges fault by the Indemnified Party, without the prior written consent of the Indemnified Party.

(d) Any indemnification hereunder for a Third Party Claim shall be made net of any insurance proceeds actually recovered by the Indemnified Party from unaffiliated Third Parties for such Third Party Claim to the extent that such insurance proceeds actually reduce the amount of such Third Party Claim; *provided, however*, that if, following the indemnification payment to the Indemnified Party of any amount under this Article VIII, such Indemnified Party recovers any such insurance proceeds in respect of the Third Party Claim for which such indemnification payment was made, the Indemnified Party shall promptly pay the Indemnifying Party an amount equal to the excess of the indemnification payment received over the amount of the indemnification payment that would have been due if the insurance proceeds had been received, realized or recovered before the indemnification payment was made.

(e) The Parties agree and acknowledge that the provisions of this Article VIII represent any Indemnified Party’s exclusive recourse with respect to any Losses for which indemnification is provided to such Indemnified Party under this Article VIII.

Section 8.4. Limitation of Liability.

No Consequential Damages. NEITHER PARTY NOR ANY OF THEIR RESPECTIVE AFFILIATES SHALL BE LIABLE TO THE OTHER PARTY OR ITS AFFILIATES FOR SPECIAL, INDIRECT, INCIDENTAL, EXEMPLARY, CONSEQUENTIAL DAMAGES OR LOSS OF PROFITS OR OPPORTUNITIES OR DIMINUTION OF GOODWILL ARISING OUT OF THIS AGREEMENT BASED ON CONTRACT, TORT OR ANY OTHER LEGAL THEORY; PROVIDED, HOWEVER, THAT NOTHING IN THIS SECTION 8.4 IS

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ARTICLE IX
TERM

Section 9.1. Term.

The term of this Agreement (the "Term") shall commence on the Effective Date and, unless earlier terminated as provided in this Article IX, shall continue in full force and effect, on a county-by-country and Licensed Product-by-Licensed Product basis until the expiration of the Royalty Term in each country in the Territory, at which time (unless earlier terminated) this Agreement shall expire with respect to such Licensed Product in such country and Fulcrum shall have a fully paid-up, royalty-free and perpetual license under the GSK Intellectual Property with respect to such Licensed Product in such country. This Agreement shall terminate in its entirety on the date this Agreement has expired with respect to all Licensed Products in all countries in the Territory.

Section 9.2. Termination for Cause.

Either Party (the "Non-Breaching Party") may, without prejudice to any other remedies available to it under Law or in equity, terminate this Agreement if the other Party (the "Breaching Party") shall have materially breached in the performance of its obligations hereunder, and such breach shall have continued for (i) [**] in the case of a breach of any obligation other than a payment obligation or (ii) [**] in the case of a breach of any payment obligation hereunder (as applicable, the "Cure Period") after written notice thereof was provided to the Breaching Party by the Non-Breaching Party, such notice describing the alleged breach. Any such termination of this Agreement under this Section 9.2 shall become effective [**] after written termination notice from the Non-Breaching Party following expiration of the Cure Period, unless the Breaching Party has cured such breach prior to the expiration of the applicable Cure Period.

Section 9.3. Effect of Termination; Accrued Rights and Obligations.

Termination of this Agreement for any reason shall not release either Party from any liability that, at the time of such termination, has already accrued or that is attributable to a period prior to such termination (including payment obligations accrued pursuant to Article III prior to the effective date of termination) nor preclude either Party from pursuing any right or remedy it may have hereunder or at Law or in equity with respect to any breach of this Agreement. It is understood and agreed that monetary damages may not be a sufficient remedy for any breach of this Agreement and that the non-breaching Party may be entitled to seek injunctive relief as a remedy for any such breach.

Section 9.4. Survival.

The rights and obligations set forth in this Agreement shall extend beyond the Term or termination of this Agreement only to the extent expressly provided for in this Agreement or to the extent required to give effect to a termination of this Agreement or the consequences of a termination of this Agreement as expressly provided for in this Agreement. Without limiting the generality of the foregoing, it is agreed that the provisions of Article I, Section 2.1, Article VI, Article VII, Article VIII, Section 9.1 (with respect to the licenses granted therein), Section 9.4 and Article X shall survive expiration or termination of this Agreement for any reason.

**ARTICLE X
MISCELLANEOUS PROVISIONS**

Section 10.1. Notices.

All notices, communications and deliveries under this Agreement will be made in writing signed by or on behalf of the Party making the same, shall specify the Section under this Agreement pursuant to which it is given or being made and shall be deemed given (a) when delivered personally, (b) when transmitted by facsimile or other electronic transmission (receipt confirmed), (c) on the close of business, local time of the recipient, on the third (3rd) Business Day after the day it is so placed in the mail or, if earlier, the time of actual receipt following mailing by registered or certified mail (return receipt requested) or (d) on the first Business Day following deposit with an overnight delivery service of national reputation, in each case to the applicable addressee at the addresses or facsimile number set forth below. Any notice that is addressed and mailed in the manner herein provided shall be conclusively presumed to have been duly given to the Party to which it is addressed.

If to GSK:

GlaxoSmithKline LLC
1250 S. Collegeville Road
Collegeville, PA 19426-0989, United States
Attention: Worldwide Business Development

with a copy to:

Vice President & Associate General Counsel
Legal- Business Development & Corporate
GlaxoSmithKline
1250 S. Collegeville Road/ UP4110
Collegeville, PA 19426-0989, United States

If to Fulcrum:

Fulcrum Therapeutics
26 Landsdowne Street

Cambridge, MA 02139
Attn: Bryan Stuart, Chief Operating Officer

With a copy to:

WilmerHale LLP
60 State Street
Boston, MA 02109
Attn: Steven D. Barrett
Telephone: (617) 526-6000
Facsimile: (617) 526-5000

Section 10.2. Schedules and Exhibits; Entire Agreement; Amendments.

The Schedules and Exhibits to this Agreement are hereby incorporated into this Agreement and are hereby made a part of this Agreement as if set out in full in this Agreement. This Agreement, together with the Schedules and Exhibits hereto, set forth all the covenants, promises, agreements, warranties, representations, conditions and understandings between the Parties hereto and supersede and terminate all prior agreements and understanding between the Parties. There are no covenants, promises, agreements, warranties, representations, conditions or understandings, either oral or written, between the Parties other than as set forth herein and therein. This Agreement may not be amended, modified or supplemented except by written agreement of the Parties expressly referencing this Agreement.

Section 10.3. Assignment.

Neither this Agreement nor any right, interest or obligation hereunder may be assigned, pledged or otherwise transferred by either Party, whether by operation of law or otherwise, without the prior consent of the other Party; *provided*, that either Party may assign its rights hereunder to (a) any of its respective Affiliates or (b) an acquirer of all or substantially all of the business or assets of such Party relating to the subject matter of this Agreement, whether by merger, sale of assets or otherwise, provided, further that in each case of (a) and (b) with respect to either Party, such Person to which such Party assigns this Agreement expressly agrees in writing to assume and be bound by all obligations of such Party under this Agreement and a copy of such written agreement by such assignee shall be provided to the other Party within [**] after such assignment.

Section 10.4. Controlling Law; Dispute Resolution.

(a) **Controlling Law.** This Agreement shall be governed by and construed and enforced in accordance with the internal laws of the State of Delaware without reference to its choice of law rules; provided, that those matters pertaining to the validity or enforceability of patent rights shall be interpreted and enforced in accordance with the laws of the territory in which such patent rights exist.

(b) Negotiation. The Parties shall endeavor to resolve in good faith any disputes or conflict arising from or relating to the subject matter of this Agreement, failing which either Party may submit such dispute for resolution to the members of their senior management as each Party may designate to handle such disputes from time to time ("Senior Management Designees"). If such Senior Management Designees are unable to resolve such dispute within [**] after such conflict is submitted to them for resolution, either Party may refer the dispute for mediation as set forth in Section 10.4(c).

(c) Mediation. If the Parties are unable to resolve a dispute arising out of or relating to this Agreement through the negotiation procedures set forth in Section 10.4(b), then at the end of such [**] period, the Parties agree to submit such dispute for confidential mediation under the CPR Mediation Procedure then in effect at the start of mediation with the International Institute for Conflict Prevention & Resolution (www.cpradr.org). Unless otherwise agreed, the Parties shall select a mediator from the CPR Panels of Distinguished Neutrals. If the Parties cannot agree, they shall defer to the CPR to select a mediator. The cost of the mediator shall be borne equally by the Parties. Any dispute not resolved within [**] (or within such other time period as may be agreed to by the Parties in writing) after appointment of a mediator shall be finally resolved by arbitration pursuant to Section 10.4(d).

(d) Arbitration. If the Parties are unable to resolve a dispute arising out of or relating to this Agreement through the negotiation procedures set forth in Section 10.4(b) and the mediation procedures set forth in Section 10.4(c) within the timeframes set forth in such Sections, the Parties agree that they shall submit such dispute for final settlement via binding arbitration. The arbitration shall be conducted under the Commercial Arbitration Rules of the American Arbitration Association in effect at the time of the arbitration, except as they may be modified herein or by mutual agreement of the Parties, but need not be under the auspices of the American Arbitration Association, and heard before a single arbitrator as selected in accordance with the Commercial Arbitration Rules. Such arbitration shall be held in Wilmington, Delaware and shall be conducted in English. Except as otherwise determined by the arbitrator, each Party shall be responsible for its own expenses in connection therewith. The arbitration award shall be final and binding upon the Parties, and judgement on the award may be entered in any court having jurisdiction thereof.

(e) For the avoidance of doubt, from the date any such dispute is referred to the Senior Management Designees in accordance with Section 10.4(b) until such time as the dispute has become finally settled or resolved, any cure periods, if applicable, shall be suspended and no termination of this Agreement by either Party as provided in this Agreement shall become effective.

(f) As between the Parties, notwithstanding anything herein to the contrary, any dispute, controversy or claim relating to the scope, validity, enforceability or infringement of any GSK Patent Rights shall not be subject to arbitration, but shall be submitted to a court of competent jurisdiction in the jurisdiction in which such Patent rights were granted or arose.

(g) Notwithstanding the Parties agreement to arbitrate, the Parties hereby agree that a Party may apply to any court of law or equity of competent jurisdiction for specific performance

or injunctive relief to enforce or prevent any violation of the provisions of Article VII of this Agreement.

Section 10.5. Severability.

Any provision of this Agreement which is prohibited or unenforceable in any jurisdiction shall, as to such jurisdiction, be ineffective to the extent of such prohibition or unenforceability without invalidating the remaining provisions of this Agreement, and any such prohibition or unenforceability in any jurisdiction shall not invalidate or render unenforceable such provision in any other jurisdiction. To the extent permitted by Law, the parties waive any provision of Law which renders any such provision prohibited or unenforceable in any respect.

Section 10.6. Counterparts.

This Agreement may be executed in two or more counterparts (delivery of which may be by facsimile, or via email as a portable document format (.pdf)), each of which will be deemed an original, and it will not be necessary in making proof of this Agreement or the terms of this Agreement to produce or account for more than one of such counterparts.

Section 10.7. No Third Party Beneficiaries.

Except for indemnification obligations hereunder to any Indemnified Party, nothing expressed or implied in this Agreement is intended, or shall be construed, to confer upon or give any Person other than the Parties, and their successors or permitted assigns, any rights, remedies, obligations or liabilities under or by reason of this Agreement, or result in such Person being deemed a third party beneficiary of this Agreement.

Section 10.8. Further Assurances.

Following the Effective Date, each of the Parties shall deliver to the other such further information and documents and shall execute and deliver to the others such further instruments and agreements as the other Party shall reasonably request to consummate or confirm the transactions provided for in this Agreement, to accomplish the purpose of this Agreement or to assure to such other Party the benefits of this Agreement.

Section 10.9. Transaction Costs.

Each Party shall bear its own expenses incident to the preparation, negotiation, execution and delivery of this Agreement and the performance of its obligations hereunder.

[Signature page follows]

IN WITNESS WHEREOF, the Parties have caused this Agreement to be duly executed, as of the date first above written.

**GLAXOSMITHKLINE INTELLECTUAL PROPERTY (NO. 2)
LIMITED**

By: /s/ Jerome Andries
Name: Jerome Andries
Title: Director

GLAXOSMITHKLINE LLC

By: /s/ Hatixhe Hoxha
Name: Hatixhe Hoxha
Title: Assistant Secretary

GLAXO GROUP LIMITED

By: /s/ John Sadler
Name: John Sadler
Title: Authorised Signatory For and on behalf Edinburgh
Pharmaceutical Industries Limited Corporate Director

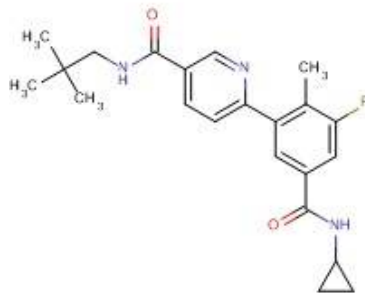
FULCRUM THERAPEUTICS, INC.

By: /s/ Robert J. Gould
Name: Robert J. Gould
Title: President & CEO

(Signature Page to Right of Reference and License Agreement)

SCHEDULE 1.1

LOSMAPIMOD COMPOUND



Formula: C₂₂H₂₆FN₃O₂

Molecular Weight: 383.459

GSK Compound Number: GW856553

SCHEDULE 1.2

GSK PATENTS

(Follows)

Case No.	Country	Application Number	Application Date	Grant Date	Patent Number
[**]	[**]	[**]	[**]	[**]	[**]

[**]

SCHEDULE 2.5(b)
SAS DATASETS

All SAS datasets related to the studies listed below (to be provided in current format):

[**]

EXHIBIT A

LETTER OF AUTHORIZATION

[GSK Letterhead]

Dear Division Director at FDA Division of Neurology Products,

Pursuant to a request from Fulcrum Therapeutics (“**Fulcrum**”), GSK hereby authorizes the United States Food and Drug Administration (“**FDA**”) to refer to the information contained in the withdrawn GSK-sponsored losmapimod INDs (IND No. [**]) in their entirety and all information therein in connection with any filing or application made by Fulcrum Therapeutics, including without limitation Fulcrum Therapeutics’ PIND [**] filing for its FTX-1821 product for treatment of Facioscapulohumeral muscular dystrophy (FSHD).

As indicated by my signature below, I am authorized to provide this authorization on behalf of GSK and my full name, title, address, email address, telephone number, are listed below.

If you have any questions, please contact me at [**].

Sincerely,

Ian Hunt
Vice President, Global Regulatory Affairs, Therapeutic Group
RD Chief Regulatory Office

GSK
1250 S. Collegeville Road, Collegeville, Pennsylvania, 19426-0989, United States
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LEASE FOR

26 LANDSDOWNE STREET

Cambridge, Massachusetts

LANDLORD

UP 26 LANDSDOWNE, LLC,
a Delaware limited liability company

TENANT

FULCRUM THERAPEUTICS, Inc.
a Delaware corporation

Dated: November 22, 2017

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ARTICLE 1

RECITALS, DEFINITIONS AND BASE LEASE TERMS

Section 1.1 **Recitals.**

This Lease (this “Lease”) is entered into this 22nd day of November, 2017 by and between UP 26 Landsdowne, LLC, a Delaware limited liability company (the “Landlord”) and Fulcrum Therapeutics, Inc., a Delaware corporation (the “Tenant”).

In consideration of the mutual covenants herein set forth, the Landlord and the Tenant do hereby agree to the terms and conditions set forth in this Lease.

Section 1.2 **Definitions.**

Certain terms used in this Lease shall have the meanings set forth below:

“Additional Rent” means all charges payable by the Tenant pursuant to this Lease other than Annual Fixed Rent, including without implied limitation the Tenant’s Tax Expense Allocable to the Premises as provided in Section 3.2; the Tenant’s Operating Expenses Allocable to the Premises in accordance with Section 3.3; amounts payable to Landlord for separately submetered utilities and services pursuant to Section 3.4; amounts payable for special services pursuant to Section 3.5; and the Landlord’s share of any sublease or assignment proceeds pursuant to Section 6.8.

“Annual Fixed Rent” - See Exhibit A and Section 3.1.

“Broker” — Jones Lang LaSalle New England LLC. See Section 12.8.

“Building” — See Exhibit A.

“Commencement Date” - See Exhibit A and Section 2.5.

“Common Areas” - See Section 2.2.

“Default Interest Rate” - see Section 9.6.

“Excusable Delay” means any delay in the satisfaction of the conditions in question to the extent the same is a consequence of External Causes including, without limitation, any governmental embargo restrictions, or actions or inactions of local, state or federal governments (such as, without limitation, any delays in issuing building permits, certificates of occupancy or other similar permits or certificates without the fault of either party).

“External Causes” means, when referring to a party’s responsibilities under this Lease, collectively Acts of God, war, civil commotion, terrorism, fire, flood or other casualty, strikes or other extraordinary labor difficulties or shortages of labor or materials or equipment in the ordinary course of trade, extraordinary weather conditions, government order or regulations or other cause not reasonably within the control of such party, and not due to the fault or neglect of such party. In no event shall financial inability be deemed to be an External Cause.

“Land” means the parcel of land situated in Cambridge, Massachusetts, described in [Exhibit B](#).

“Landlord’s Address for Notices”

UP 64 Sidney Street, LLC
c/o Forest City Enterprises, Inc.
1130 Terminal Tower
50 Public Square
Cleveland, Ohio 44113-2203
Attention: President

with copies to:

Forest City Commercial Management, Inc.
38 Sidney Street
Cambridge, Massachusetts 02139-4234
Attention: General Manager

“Landlord’s Work” — See Section 2.1

“Leasehold Improvements” — See [Exhibit E-1](#).

“Lease Commencement Date” - See [Exhibit A](#) and Section 2.5.

“Lease Year” — A one year period commencing on the Rent Commencement Date (provided, however, that if the Rent Commencement Date does not occur on the first day of a month, the first Lease Year shall end on the last day of the month in which the anniversary of the Rent Commencement Date occurs); each subsequent Lease Year shall consist of one calendar year beginning on the day immediately following the expiration of the prior Lease Year.

“Park” — The buildings and associated land located from time to time within University Park at MIT, as such area is depicted on [Exhibit C-2](#).

“Parking Passes” — See [Exhibit A](#)

“Permitted Uses: - See [Exhibit A](#).

“Premises: - See [Exhibit A](#).

“Property” — The Land and the Building.

“Removable Alterations” - See Section 4.2.

“Rules and Regulations” - See Section 6.3 and Exhibit F.

“Tenant’s Original Address” — see Exhibit A.

“Tenant’s Work” — See Section 4.3.

“Term” — See Exhibit A.

Section 1.3 Base Lease Terms.

The Basic Lease Terms are set forth on Exhibit A, attached.

ARTICLE 2

PREMISES AND TERM

Section 2.1 Premises.

The Landlord hereby leases to the Tenant, and the Tenant hereby leases from the Landlord, for the Term, the Premises comprised of the space illustrated on Exhibit C-1, in its current as-is condition, except for (i) completion of work required by Landlord to fulfill Landlord’s obligations as outlined in the Tenant/Landlord Responsibility Matrix attached hereto as Exhibit D provided the parties acknowledge and agree that Landlord’s Work shall proceed concurrently with the construction of Tenant’s Work (to the extent that such Landlord’s Work does not materially interfere with the construction of Tenant’s Work); (ii) demolition and disposal of the existing improvements in the Premises, (iii) installation of a new centralized lab-ready base building HVAC system, delivery of mechanical electrical, life safety and plumbing systems serving the Premises in good operating condition and repair, and (iv) refurbish the existing common area locker and common shower room on the first floor of the Building (all work described in (i) — (iv) above, collectively, the “Landlord’s Work”) subject to the exclusion herein below set forth in this Section 2.1, Landlord’s reservations set forth in Section 2.3, such easements, covenants and restrictions as may affect the Property and the terms and conditions of this Lease . Landlord shall perform the Landlord’s Work in a good and workmanlike manner, free from faults and defects, in compliance with all applicable federal, state and local laws, rules and regulations.

Landlord shall complete the Landlord’s Work in a timely and diligent manner and in accordance with the Construction Schedule set forth at Exhibit M, and with the completion of the Landlord’s Work scheduled to occur no later than May 31, 2018 (the “**Landlord’s Work Target Date**”). In the event that Landlord has not completed Landlord’s Work by July 15, 2018 (the “**Initial Delivery Deadline**”), subject in each case to extension for each day of Tenant Delay

pursuant to the Work Letter, Tenant shall be entitled to one (1) day of abatement of Annual Fixed Rent for each day of such delay. Completion of Landlord's Work shall be achieved when such work is complete except for Punch List (as defined below) items that do not adversely affect Tenant's Use and occupancy of the Premises, all utilities, building systems and equipment, including without limitation the HVAC systems and components, are in good working order and Landlord has received a certificate of occupancy from the applicable authority of the City of Cambridge for Landlord's Work (excluding the Tenant Improvements). In the event that Landlord has not completed Landlord's Work within forty-five (45) days after the Initial Delivery Deadline, then Tenant shall be entitled to two (2) days of abatement of Annual Fixed Rent for each day of such delay. In the event that Landlord has not completed Landlord's Work within one hundred thirty-five (135) days after the Initial Delivery Deadline (herein, the "**Outside Delivery Deadline**"), subject to extension for each day of Tenant Delay pursuant to the Work Letter, this Lease may be terminated by Tenant, effective upon written notice delivered to Landlord no later than the date that is ten (10) days after such Outside Delivery Deadline. If Tenant has not delivered such written notice of termination to Landlord within such required time period, then this Lease shall remain in full force and effect. If Tenant delivers such written notice of termination within such required time period, then the Security Deposit, or any balance thereof (i.e., after deducting therefrom all amounts to which Landlord is entitled under the provisions of this Lease), shall be returned to Tenant, and neither Landlord nor Tenant shall have any further rights, duties or obligations under this Lease, except any provisions which expressly survive termination of this Lease.

Landlord shall use good faith efforts to ensure, and cause Contractor to ensure, that completion of the Landlord's Work shall not interfere with the ongoing construction of the Initial Leasehold Improvements. See Section 4.5 herein for additional requirements governing the Landlord's Work. On or before the anticipated Rent Commencement Date, Tenant or Tenant's representative shall conduct an inspection of the Premises with Landlord or Landlord's representative to develop a punch list of all Landlord's Work items which are not complete or which require correction (the "Punch List"). Landlord shall complete and/or correct all items on the Punch List within thirty (30) days after Landlord receives the Punch List and shall give Tenant written notice when all of the items on the Punch List have been completed and/or corrected.

Landlord warrants, for a period of one year from the date of completion of Landlord's Work as provided in this Section, that Landlord's Work shall be constructed (i) in a good and workmanlike manner and with all utilities, building systems and equipment, including without limitation the HVAC systems and components, in good working order (such warranty shall be exclusive of equipment warranties provided directly by manufacturers for equipment to be installed within the Premises as provided below), (ii) in compliance with applicable legal requirements, and (iii) substantially in accordance with the plans and specifications therefor (collectively, "**Landlord's Warranty**"). Tenant shall have one year after the date of completion of Landlord's Work as provided in this Section within which to notify Landlord of any breach of Landlord's Warranty (a "**Construction Defect**"). Within 30 days after delivery Tenant's notice of any such Construction Defect, Landlord shall remedy or cause the responsible contractor to remedy any such Construction Defect within a reasonable time.

Tenant shall be entitled to receive the benefit of all construction warranties and manufacturer's equipment warranties relating to equipment installed in the Premises. If requested by Tenant, Landlord shall attempt to obtain extended warranties from manufacturers and suppliers of such equipment, but the cost of any such extended warranties shall be borne by Tenant or payable out of the LIA (as defined in the Work Letter).

Tenant shall further be subject to any easements, covenants and/or restrictions or other matters of record encumbering the Park provided that any such matters of record arising after the date hereof do not prohibit Tenant's use and occupancy of the Premises for the Permitted Use or materially and adversely affect Tenant's rights under this Lease. The Tenant acknowledges that, except as expressly set forth in this Lease, there have been no representations or warranties made by or on behalf of the Landlord with respect to the Premises, the Building or the Property or with respect to the suitability of any of them for the conduct of the Tenant's business or activities. The Premises shall exclude common areas and facilities of the Property, including without limitation exterior faces of exterior walls, the entry, vestibules and main lobby of the Building, first floor elevator lobby and lavatories, the common stairways and stairwells, elevators and elevator wells, boiler room, sprinklers, sprinkler rooms, elevator rooms, mechanical rooms, loading and receiving areas, electric and telephone closets, janitor closets, and pipes, ducts, conduits, wires and appurtenant fixtures and equipment serving exclusively or in common other parts of the Building. If the Premises at any time includes less than the entire rentable floor area of any floor of the Building, the Premises shall also exclude the common corridors, vestibules, elevator lobby, lavatories, and freight elevator vestibule located on such floor. Landlord shall be delivering the Premises in "as is" condition at the Commencement Date of the Lease. Prior to the Commencement Date, Landlord shall provide Tenant with evidence of the decommissioning of the Premises by the prior tenant.

Landlord represents and warrants to Tenant that, to the best of Landlord's current knowledge, information, and belief, (a) the Building and the Premises are in material compliance with all applicable zoning, land use and environmental laws and agreements, the Americans with Disabilities Act of 1990, as amended, and the requirements of all easement and encumbrance documents and Landlord covenants to keep the Building in compliance throughout the Term; (b) Landlord holds the tenant's interest under the Ground Lease (as such term is defined in Section 12.14), subject to no mortgage other than the current mortgage to CIGNA; (c) Landlord has full power and authority to enter into this Lease and has obtained all consents and taken all actions necessary in connection therewith; and (d) no other party has any possessory right to the Premises or has claimed the same.

Section 2.2 Appurtenant Rights.

(a) The Tenant shall have, as appurtenant to the Premises, the nonexclusive right to use in common with others, subject to the Rules and Regulations (as defined in Section 6.3): (i) the entry, vestibules, main lobby and common locker room/shower room on the first level of the Building, the common stairways, elevators, sprinkler rooms, mechanical rooms, electric and telephone closets, and the pipes, sprinklers, ducts, conduits, wires and appurtenant fixtures and equipment serving the Premises in common with others, (ii) common walkways and driveways situated upon the Land that are necessary or reasonably convenient for access to the Building, (iii) access to, and use of in common with other tenants of, loading and receiving areas

and freight elevators, and electrical and telephone closets, all subject to Rules and Regulations then in effect and (iv) if the Premises at any time includes less than the entire rentable floor area of any floor, the common corridors, vestibules, elevator lobby, lavatories, and freight elevator vestibule located on such floor (collectively, the "Common Areas"). Without limiting the foregoing, Tenant shall have as appurtenant to the Premises, (A) the right to use a portion of the first floor to house Tenant's acid neutralization system (which shall be operated and maintained by Tenant), together with access thereto from the common hallway, (B) use of the central vacuum system and compressed air system in common with other tenants entitled thereto, together with access to such systems, and (C) the right to use Tenant's Share of the Building's solvent storage capacity of 480 gallons and access to the control areas therefor as more fully provided in Section 12.16 hereof. Tenant shall have 24-hour, seven (7) days per week access to the Premises, the space where Tenant's acid neutralization system is located, the common central vacuum and compressed air systems, control areas for solvent storage, freight loading docks and freight elevators, and the dumpster and/or compactor provided by Landlord in the refuse disposal area, subject to the provisions of this Lease and interruption for External Causes, casualty and condemnation.

(b) Subject to Section 4.1 with respect to installation requirements, Tenant shall have the right, at no additional rental cost, to install heating, ventilation and air conditioning equipment, generators, antennas, satellite dishes and other equipment on the roof of the Building in areas that in aggregate do not exceed Tenant's proportionate share of roof area of the Building, in each case in locations designated by Landlord. Any such equipment installed by Tenant shall be for Tenant's own use and shall be subject to (i) Landlord's approval regarding location and installation specification, and such requirements intended to any specifications arising from the roof warranty, including the requirement to use such contractor(s) as Landlord may specify for such work, such approval not to be unreasonably withheld, conditioned or delayed, and (ii) applicable City of Cambridge and other legal requirements. Tenant shall be responsible for all costs relating to the installation, maintenance and removal of such equipment installed by Tenant on the Building roof.

Section 2.3 Landlord's Reservations.

(a) The Landlord reserves the right from time to time, without unreasonable interference with the Tenant's use to alter or modify the Common Areas, provided that (i) the Landlord gives the Tenant reasonable advance notice of the Landlord's contemplated alterations or modifications where they are reasonably likely to impact Tenant's use and enjoyment of the Premises, (ii) any such actions are effected in a good and workmanlike manner, and (iii) such alterations or modifications do not permanently impair Tenant's access to the Premises or its practical use and enjoyment thereof or of the Appurtenant Rights.

(b) In addition to other rights reserved herein or by law, Landlord reserves the right from time to time, without unreasonable interruption of Tenant's use and access to the Premises (and in any event during the existence of an emergency) (i) to make additions to or reconstructions of the Building and to install, use, maintain, repair, replace and relocate for service to the Premises and other parts of the Building, the pipes, ducts, conduits, wires and appurtenant fixtures, wherever located in the Premises, the Building, or elsewhere in the Property, provided that, to the extent practicable such installations, replacements or relocations

in the Premises shall be placed above ceiling surfaces, below floor surfaces, or to the outside of the interior face of perimeter walls; (ii) to name or change the name of the Building, and (iii) to grant easements and other rights with respect to the Property.

Section 2.4 Parking Passes.

From and after the Rent Commencement Date, the Landlord shall provide Parking Passes (as defined in Exhibit A) for use by the Tenant's employees in accordance with the provisions of this Section 2.4, and in the 55 Franklin Street garage as designated on Exhibit C-2. Landlord reserves the right to relocate some or all of Tenant's parking spaces to other parking garages within University Park, which relocation right shall not be exercised by Landlord more than twice in any twelve (12)-month period. The Tenant agrees that it and all persons claiming by, through and under it, shall at all times abide by the Rules and Regulations with respect to the use of the parking facilities provided by the Landlord pursuant to this Lease. The Landlord acknowledges that it is the Landlord's responsibility to assure Tenant that holders of Parking Passes who comply with the Rules and Regulations are able to park their motor vehicles in the designated parking facilities within the Park. The Tenant acknowledges that the parking facilities within the Park may be owned by an entity other than Landlord. In no event are Parking Passes transferable other than to the holder, from time to time, of the tenant's interest under this Lease or a subtenant that has been demised all or a portion of the Premises in conformity with the requirements of this Lease. Parking Passes are limited to use by employees of either of the foregoing.

The parking spaces relating to the Parking Passes shall be accessible twenty four (24) hours per day, seven (7) days per week. In no event are Parking Passes transferable other than to the holder, from time to time, of the tenant's interest under this Lease or a subtenant that has been demised all or a portion of the Premises in conformity with the requirements of this Lease, and use of the Parking Pass is limited to use by employees, business invitees and visitors of either of the foregoing. The charge for each Parking Pass shall be equal to the Market Rate Parking Charge, established by the parking garage operator from time to time. "Market Rate Parking Charge" means the monthly parking rate for parking facilities charged from time to time by owners of parking facilities of comparable quality at mixed use office/research parks in the commercial markets that surround the MIT campus (East Cambridge/Kendall Square/Cambridgeport). The Market Rate Parking Charge shall constitute Additional Rent and shall be payable monthly to Landlord at the time and in the fashion in which Annual Fixed Rent under this Lease is payable. Without limiting Landlord's other remedies under the Lease, if Tenant shall fail to pay the amounts due for such Parking Passes for more than thirty (30) days after notice of such failure, then Landlord may terminate Tenant's rights to such Parking Passes immediately upon notice by Landlord.

Upon written request from time to time, and subject to availability (as determined by Landlord in its sole discretion), Tenant may obtain additional Parking Passes on a month-to-month basis (i.e. terminable by either party on 30 days' prior written notice), which additional Parking Passes shall be provided to Tenant on all of the terms and conditions of this Article 2 except as expressly set forth in this sentence.

At any time during the Term Landlord shall have the right to assign Landlord's obligations to provide parking, as herein set forth, together with Landlord's right to receive Additional Rent for such parking spaces as herein provided, to a separate entity created for the purpose of providing the parking privileges set forth herein. In such event, Landlord and Tenant agree to execute and deliver appropriate documentation, including documentation with the new entity, reasonably necessary to provide for the new entity to assume Landlord's obligations to provide the parking privileges to Tenant as specified herein and for the Tenant to pay the Additional Rent attributable to the parking privileges directly to the new entity. Landlord shall, however, remain primarily liable for the provision of Tenant's parking privileges.

Section 2.5 Lease Commencement Date, Landlord Delivery Date and Rent Commencement Date.

The "Lease Commencement Date" and the "Landlord Delivery Date" shall be the date that Landlord delivers the Premises to Tenant in broom-clean shell condition, with all demolition associated with existing leasehold improvements complete and with the Premises in a condition to allow Tenant to commence the Tenant Work ("Tenant Construction Readiness"). The Landlord shall give written notice to Tenant as to the Landlord Delivery Date no less than ten (10) days prior to such Landlord Delivery Date, and the Landlord shall cause the Landlord Delivery Date to be no earlier than November 1, 2017 and no later than January 1, 2018. In the event that the Landlord Delivery Date has not occurred by February 15, 2018 (the "**Outside Readiness Deadline**"), subject in each case to extension for each day of Tenant Delay pursuant to the Work Letter, Tenant shall be entitled to one (1) day of abatement of Annual Fixed Rent for each day of such delay. In the event that Landlord has not completed Landlord's Work within forty-five (45) days after the Outside Readiness Deadline, then Tenant shall be entitled to two (2) days of abatement of Annual Fixed Rent for each day of such delay. In the event that the Landlord Delivery Date has not occurred within one hundred thirty-five (135) days after the Outside Readiness Deadline, subject to extension for each day of Tenant Delay pursuant to the Work Letter, this Lease may be terminated by Tenant, effective upon written notice delivered to Landlord no later than the date that is ten (10) days after such one hundred thirty-fifth (135th) day after the Outside Readiness Deadline. If Tenant has not delivered such written notice of termination to Landlord within such required time period, then this Lease shall remain in full force and effect. If Tenant delivers such written notice of termination within such required time period, then the Security Deposit, or any balance thereof (i.e., after deducting therefrom all amounts to which Landlord is entitled under the provisions of this Lease), shall be returned to Tenant, and neither Landlord nor Tenant shall have any further rights, duties or obligations under this Lease, except any provisions which expressly survive termination of this Lease.

The "Rent Commencement Date" shall be the earlier to occur of (i) Tenant's occupancy of any portion of the Premises for business purposes, or (ii) six (6) months after the Landlord Delivery Date (the "Scheduled Rent Commencement Date"). Notwithstanding the foregoing, upon the following terms and conditions, but not otherwise, if (i) the Landlord is delayed in achieving (a) Tenant Construction Readiness beyond the Tenant Construction Readiness Date, or (b) Substantial Completion of the Landlord's Work beyond the Landlord's Work Target Date, or (ii) the Tenant is delayed in Tenant's Construction Work by a Landlord Delay and (iii) any such delay is not due to Tenant Delay, then the Scheduled Rent Commencement Date shall be postponed by the number of days that Tenant Construction Readiness and/or Substantial

Completion of the Landlord's Work is so delayed. Without limitation of the foregoing, there shall be no postponement of the Scheduled Rent Commencement Date to the extent that the Tenant Construction Readiness Date, the Substantial Completion of the Landlord's Work or Tenant's Construction Work is delayed on account of Tenant Delay.

The Lease Commencement Date, the Rent Commencement Date, and the Term shall be as set forth on Exhibit A.

Section 2.6 Extension Option.

Provided that there has been no Event of Default which is uncured and continuing on the part of the Tenant, and the Tenant or any entity which succeeds to Tenant's rights hereunder pursuant to a Permitted Transfer is, as of the date of exercise and as of the commencement date of each Extension Term, actually occupying at least seventy-five percent (75%) of the Premises for its business purposes, the Tenant shall have the right to extend the Term hereof for one (1) additional period of five (5) years on the following terms and conditions (the "Extension Option):

(a) The Tenant shall have the right to extend the Term hereof for one (1) period of five (5) years (the "Extension Term") on the terms and conditions set forth in this Section 2.6(a) and (b). "Such right to extend the Term shall be exercised by the giving of notice by Tenant to Landlord at least nine (9) months prior to the expiration of the Initial Term (the "Extension Notice Deadline Date"). Upon the giving of such notice on or before the Extension Notice Deadline Date, this Lease and the Term hereof shall be extended for an additional term of five (5) years, without the necessity for the execution of any additional documents except a document memorializing the Annual Fixed Rent for the Extension Term to be determined as set forth below. Time shall be of the essence with respect to the Tenant's giving notice to extend the Term on or before the Extension Notice Deadline Date.

(b) The Extension Term shall be upon all the terms, conditions and provisions of this Lease except the Annual Fixed Rent during first Lease Year of the Extension Term shall be the then Extension Fair Rental Value of the Premises for the Extension Term to be determined under Section 2.6(c) below with respect to which the Extension Fair Rental Value is to be established (the "Then Applicable Annual Fixed Rental Rate"). If the Tenant makes a written request to the Landlord for a proposal for the Extension Fair Rental Value for the Extension Term, the Landlord shall make such a written proposal to the Tenant within thirty (30) days after receipt of the Tenant's request therefor, but in no event shall the Landlord be required to deliver such a proposal sooner than twelve (12) months prior to the date as of which such proposal is to become effective. Alternatively, the Landlord may, at its election, propose an Extension Fair Rental Value to the Tenant without any request having been made. The determination of the Extension Fair Rental Value shall include a determination as to whether an Annual Fixed Rent Escalator Factor should be applicable to the Extension Term, and, if so, the amount thereof.

(c) For purposes of this Section 2.6, the Extension Fair Rental Value of the Premises shall mean the then current fair market annual rent for leases of other space similarly improved, taking into account all relevant factors, including but not limited to the condition to which such premises have been improved, the economic terms and conditions specified in this

Lease that will be applicable thereto, for comparable laboratory and office space located in the commercial markets that surround the MIT campus (East Cambridge, Kendall Square, and Cambridgeport). The Landlord and the Tenant shall endeavor in good faith to agree upon the Extension Fair Rental Value of the Premises within thirty (30) days after the Tenant has exercised its option for the Extension Term. If the Extension Fair Rental Value of the Premises is not agreed upon by the Landlord and the Tenant within this time frame, each of the Landlord and the Tenant shall retain a real estate professional with at least ten (10) years continuous experience in the business of appraising or marketing similar commercial real estate in the Cambridge, Massachusetts area who shall, within thirty (30) days of his or her selection, prepare a written report summarizing his or her conclusion as to the Extension Fair Rental Value. The Landlord and the Tenant shall simultaneously exchange such reports; provided, however, if either party has not obtained such a report within said thirty (30) day period then the determination set forth in the other party's report shall be final and binding upon the parties. If both parties receive reports within such time and the lower determination is within ten percent (10%) of the higher determination, then the average of these determinations shall be deemed to be the Extension Fair Rental Value for the Premises. If these determinations differ by more than ten percent (10%), then the Landlord and the Tenant shall mutually select a person with the qualifications stated above (the "Final Professional") to resolve the dispute as to the Extension Fair Rental Value for the Premises. If the Landlord and the Tenant cannot agree upon the designation of the Final Professional within thirty (30) days of the exchange of the first valuation reports, either party may apply to the American Arbitration Association, the Greater Boston Real Estate Board, or any successor thereto, for the designation of a Final Professional. Within ten (10) days of the selection of the Final Professional, the Landlord and the Tenant shall each submit to the Final Professional a copy of their respective real estate professional's determination of the Extension Fair Rental Value for the Premises. The Final Professional shall not perform his or her own valuation, but rather shall, within thirty (30) days after such submissions, select the submission which is closest to the determination of the Extension Fair Rental Value for the Premises which the Final Professional would have made acting alone. The Final Professional shall give notice of his or her selection to the Landlord and the Tenant and such decision shall be final and binding upon the Landlord and the Tenant. Each party shall pay the fees and expenses of its real estate professional and counsel, if any, in connection with any proceeding under this paragraph, and one-half of the fees and expenses of the Final Professional. In the event that the commencement of the Extension Term occurs prior to a final determination of the Extension Fair Rental Value therefor (the "Extension Rent Determination Date"), then the Tenant shall pay the Annual Fixed Rent at Annual Fixed Rental Rate for the last day of the Term prior to the commencement of such extension. If the Annual Fixed Rent for the Extension Term is determined to be greater than the Annual Fixed Rent paid with respect to the Premises prior to the Extension Rent Determination Date, then the Tenant shall pay to the Landlord the amount of such underpayment within ten (10) days of the Extension Rent Determination Date, and if the Annual Fixed Rent for the Extension Term is determined to be less than the Annual Fixed Rent paid with respect to the Premises prior to the Extension Rent Determination Date, then the Landlord shall credit the amount of such overpayment against the monthly installments of Annual Fixed Rent thereafter coming due.

ARTICLE 3

RENT AND OTHER PAYMENTS

Section 3.1 Annual Fixed Rent.

The Annual Fixed Rent applicable to the Premises during the Term shall be as set forth on Exhibit A. On the Rent Commencement Date and on the first day of each month thereafter, the Tenant shall pay, without notice or demand, monthly installments of one twelfth (1/12) of the Annual Fixed Rent in effect in advance for each full calendar month of the Term following the Rent Commencement Date and a corresponding fraction of said one twelfth (1/12) for any fraction of a calendar month in which the Rent Commencement Date occurs. On the day that is the first anniversary of the Rent Commencement Date, and on each anniversary of that date thereafter, Annual Fixed Rent for the Premises shall increase to an amount equal to one hundred three percent (103%) of the Annual Fixed Rent immediately preceding such anniversary.

Section 3.2 Real Estate Taxes.

From and after the Rent Commencement Date, during the Term, the Tenant shall pay to the Landlord, as Additional Rent, the Tenant's Tax Expenses Allocable to the Premises (as such term is hereinafter defined) in accordance with this Section 3.2. The terms used in this Section 3.2 are defined as follows:

- (a) "Tax Fiscal Year" means the 12 month period beginning on the first date of the fiscal period in respect of which real estate taxes are due and payable to the appropriate governmental taxing authority.
- (b) "The Tenant's Tax Expense Allocable to the Premises" means (i) that portion of the Landlord's Tax Expenses for an Operating Fiscal Year (as defined below) which bears the same proportion thereto as the rentable floor area of the Premises (from time to time) bears to the rentable floor area of the Building and (ii) in the event that the Premises are improved to a standard which is materially higher than other portions of the Property and the taxing authority has calculated the Building valuation on such basis as provided in the notice of such new valuation or reassessment, such portion of the Real Estate Taxes on the Property with respect to any Operating Fiscal Year as is appropriate so that the Tenant bears the portion of the Real Estate Taxes which are properly allocable to the Premises, as reasonably determined by Landlord based on information with respect to the assessment process made available by the assessing authorities. Notwithstanding the foregoing, laboratory improvements made to the Premises that are typical in a Class A laboratory building in Cambridge shall not be deemed to result in the Premises being improved to a standard which is materially higher than other portions of the Property.
- (c) "The Landlord's Tax Expenses" with respect to any Tax Fiscal Year means the aggregate Real Estate Taxes with respect to that Tax Fiscal Year, reduced by any abatement receipts with respect to that Tax Fiscal Year.
- (d) "Real Estate Taxes" means (i) all taxes, assessments and similar charges of every kind and nature assessed by any governmental authority on the Property; (ii) reasonable

expenses incurred in connection with negotiating with the city assessor's office, in advance of the establishment of the assessed valuation of the Property, to establish a fair and reasonable assessment therefor; and (iii) reasonable expenses incurred in connection with any proceedings for abatement of such taxes or special assessments. Any special assessments to be included within the definition of "Real Estate Taxes" shall be limited to the amount of the installment (plus any interest thereon) of such special tax or special assessment (which shall be payable over the longest period permitted by law as reasonably determined by Landlord) required to be paid during the Operating Fiscal Year in respect of which such taxes are being determined. Without limiting the foregoing, Real Estate Taxes include any payments in lieu of taxes. There shall be excluded from such taxes all income, estate, succession, inheritance, excess profit, franchise and transfer taxes, and delinquency interest or penalties; provided, however, that if at any time during the Term the present system of ad valorem taxation of real property shall be changed so that in lieu of the whole or any part of the ad valorem tax on real property, there shall be assessed on the Landlord a capital levy or other tax on the gross rents received with respect to the Property, or a federal, state, county, municipal or other local income, franchise, excise or similar tax, assessment, levy or charge (distinct from any now in effect) based, in whole or in part, upon any such gross rents, then any and all of such taxes, assessments, levies or charges, to the extent so based, shall be deemed to be included within the term "Real Estate Taxes," based on the Property being the Landlord's only property. Landlord may elect to allocate Real Estate Taxes separately among tenants with different use categories in the Building from time to time based on such factors as the Landlord reasonably determines (rather than on a proportionate basis based on square feet) if Landlord reasonably determines it is necessary to fairly allocate the Real Estate Taxes, provided that Landlord will not allocate Real Estate Taxes separately for any tenant whose use includes laboratory or research and development use along with office or other uses but may allocate Real Estate Taxes separately for tenants whose use is solely office use or solely retail use.

Payments by the Tenant on account of the Tenant's Tax Expense Allocable to the Premises shall be made monthly at the time and in the fashion herein provided for the payment of Annual Fixed Rent and shall be in an amount of the greater of (i) one twelfth (1/12) of the Tenant's Tax Expense Allocable to the Premises for the current Operating Fiscal Year as reasonably estimated by the Landlord, or (ii) an amount reasonably estimated by any holder of a first mortgage or similar lien on the Property, to be sufficient, if paid monthly, to pay the Tenant's Tax Expense Allocable to the Premises on the dates due to the taxing authority.

Not later than one hundred twenty (120) days after the end of each Operating Fiscal Year or fraction thereof at the end of during the Term, the Landlord shall render the Tenant a statement in reasonable detail showing for the preceding Tax Fiscal Year of the Term or fraction thereof, as the case may be, real estate taxes on the Property, and any abatements or refunds of such taxes, together with a copy of the tax bill or bills for the Tax Fiscal Year in question. Reasonable expenses incurred in obtaining any tax abatement or refund not previously charged may be charged against such tax abatement or refund before the adjustments are made for the Tax Fiscal Year. If at the time such statement is rendered it is determined with respect to any Operating Fiscal Year, that the Tenant has paid (i) less than the Tenant's Tax Expense Allocable to the Premises or (ii) more than the Tenant's Tax Expense Allocable to the Premises, then, in the case of (i) the Tenant shall pay to the Landlord, as Additional Rent, within thirty (30) days of such statement the amount of such underpayment and, in the case of (ii) the Landlord shall credit

the amount of such overpayment against the monthly installments of the Tenant's Tax Expense Allocable to the Premises next thereafter coming due (or refund such overpayment within thirty (30) days if the Term has expired to the extent that such overpayment exceeds any amount then due from the Tenant to the Landlord). To the extent that real estate taxes shall be payable to the taxing authority in installments with respect to periods less than a Tax Fiscal Year, the statement to be furnished by the Landlord shall be rendered and payments made on account of such installments. Landlord shall, upon Tenant's request, provide Tenant with a copy of all applicable tax bills, statements, records and the like, as well as any reasonably relevant supporting documentation in Landlord's possession. If the Commencement Date occurs on other than the first day of an Operating Fiscal Year, or if the Termination Date occurs on other than the last day of an Operating Fiscal Year, then the amount of Tenant's Tax Expense Allocable to the Premises payable by the Tenant with respect to such Operating Fiscal Year(s) shall be prorated based upon the ratio of the length of the time period during such Operating Fiscal Year(s) in respect of which the Tenant has an obligation to pay Tenant's Tax Expense Allocable to the Premises to the length of such Operating Fiscal Year(s).

Section 3.3 Operating Expenses.

From and after the Rent Commencement Date, during the Term, the Tenant shall pay to the Landlord, as Additional Rent, the Tenant's Operating Expenses Allocable to the Premises, in accordance with this Section 3.3 including, without limitation, the conditions and limitations set forth in clauses (a) through (l) below, with respect to each twelve (12) month period beginning January 1 each year or such other fiscal period of twelve (12) consecutive months hereinafter adopted by the Landlord for lease administration purposes ("Operating Fiscal Year"). Subject to the provisions of this Section 3.3, "The Tenant's Operating Expenses Allocable to the Premises" means that portion of the Operating Expenses for the Property which bears the same proportion thereto as the rentable floor area of the Premises bears to the rentable floor area of the Building. The term "Operating Expenses for the Property" means the Landlord's actual cost of managing, operating, cleaning, maintaining and repairing the Property, including the roads, driveways and walkways providing access to the Building, and shall include without limitation, the cost of fulfilling the maintenance and repair obligations required to be performed by Landlord under Section 5.1 and, subject to the exclusions set forth below, the cost of services performed by Landlord and specified on Exhibit E; premiums for insurance carried pursuant to Section 7.4; the amount of any deductible associated with an insurance claim of the Landlord; compensation (including, without limitation, fringe benefits, worker's compensation insurance premiums and payroll taxes) paid to, for or with respect to all persons engaged in the managing, operating, maintaining or cleaning the Property; legal, auditing, consulting, and professional fees and other costs incurred in connection with the normal and routine maintenance and operation of the Building; interior landscaping and maintenance; steam, water, sewer, gas, oil, electricity, telephone and other utility charges (excluding any such utility charges either separately metered or separately chargeable to the Tenant); cost of providing HVAC services; cost of building and cleaning supplies; the costs of routine environmental and energy efficiency management programs operated by Landlord; market rental costs (or alternatively the Amortization Charge Off (as hereinafter defined) so long as the expenses which are the subject of such Amortization Charge Off would have been permitted Operating Expenses had the item in question been purchased) with respect to equipment used in managing, operating, cleaning, maintaining or repairing the Property; cost of cleaning; cost of maintenance and non-capital repairs and

replacements; cost of snow removal; cost of landscape maintenance; cost of security services; payments under service contracts with independent contractors; management fees at reasonable rates consistent with comparable multi-tenant buildings, as applicable, in the submarket within which the Premises is located with the type of occupancy and services rendered, not to exceed three percent (3%) of Annual Fixed Rent in any year; the cost of any capital repairs, replacements or improvements which (i) are required by any law or regulation enacted or promulgated after the date of this Lease, (ii) reduce Operating Expenses, or (iii) improve the management and operation of the Property or the Common Areas in a manner reasonably acceptable and consented to by Tenant in writing in advance of such expenditure (all such capital costs to be amortized on a straight line basis in accordance with generally accepted accounting principles, together with interest on the unamortized balance at such rate as may have been paid by the Landlord on funds borrowed for the purpose of making such capital repairs, replacements or improvements (or if the Landlord did not borrow such funds, then at the base lending rate announced by a major commercial bank designated by the Landlord), with only the annual amortization amount ("Amortization Charge Off") being included in Operating Expenses with respect to any Operating Fiscal Year); charges equitably and reasonably allocated to the Building for the operating, cleaning, maintaining, securing and repairing of the Common Areas excluding the initial capital improvement costs associated with initially establishing the Common Areas; costs incurred by Landlord in connection with any employee transportation assistance consisting of shuttle service between the Park and public transportation; and all other reasonable and necessary (in the Landlord's reasonable judgment) expenses paid in connection with the operation, cleaning, maintenance and repair of the Property and Common Areas.

If less than ninety-five percent (95%) of the total rentable floor area of the Building is occupied at any time during the term of this Lease, Landlord may extrapolate components of Operating Expenses that vary with occupancy as though ninety-five percent (95%) of the total rentable floor area of the Building had been occupied at all times during such period, but only if such expenses are actually expended. Additionally, Tenant shall not be charged for amounts allocable to vacant space.

Operating Expenses for the Property shall not include the following:

- (a) any cost or expense to the extent to which Landlord is paid or reimbursed, or which is reimbursable to the Landlord, from a third party (other than as a payment for Operating Expenses), insurance, warranties, service contracts, condemnation proceeds or similar sources;
- (b) salaries and bonuses of officers or executives of Landlord or administrative employees above the grade of the Building general manager, and if personnel below such grades are shared with other buildings or have other duties not related to the Building, only the allocable portion of such person or persons salary shall be included in Operating Expenses;
- (c) interest on debt or principal amortization payments (except as expressly otherwise provided) or any other payments on any mortgage or any payments under any ground lease;

(d) any fees, costs, and commissions incurred in procuring or attempting to procure other tenants including, but not necessarily limited to brokerage commissions, finders' fees, attorneys' fees and expenses, entertainment costs and travel expenses, marketing costs, attorneys' fees in connection with the negotiation and preparation of letters, deal memos, letters of intent, leases, subleases and/or assignments), space planning costs, and other costs and expenses incurred in connection with lease, sublease and/or assignment negotiations and transactions with present or prospective tenants or other occupants of the Building;

(e) any cost included in Operating Expenses representing an amount paid to a person, firm, corporation or other entity related to Landlord which is in excess of the amount which would have been paid on an arms' length basis in the absence of such relationship (provided that nothing herein shall be construed as requiring that the cost in question equal the lowest possible cost; only that the cost not be inflated solely due to the absence of an arms' length relationship);

(f) depreciation of the Building or any part thereof;

(g) any costs incurred for services or maintenance attributable to portions of the Park which Tenant does not have the right to use;

(h) any costs attributable to the parking garages within University Park;

(i) costs which may be considered capital improvements, capital repairs, capital changes or any other capital costs as determined under generally accepted accounting principles except for the Amortization Charge Off;

(j) advertising and promotional expenditures, and costs of acquisition and maintenance of signs in or on the Building identifying the owner of the Building or other tenants;

(k) costs, including permit, license and inspection costs, incurred with respect to the installation of other tenants' or other occupants' improvements or incurred in renovating or otherwise improving, decorating, painting or redecorating vacant space for tenants or other occupants of the Building;

(l) expenses in connection with services or other benefits which are not offered to Tenant or for which Tenant is charged for directly;

(m) costs incurred by Landlord due to the violation by Landlord or any tenant of the terms and conditions of any lease of space in the Building;

(n) amounts paid to Landlord or to subsidiaries or affiliates of Landlord for goods and/or services in the Building to the extent the same exceeds the costs of such goods and/or services rendered by unaffiliated third parties on a competitive basis;

(n) Landlord's general corporate overhead and corporate administrative expenses;

- (o) any compensation paid to clerks, attendants or other persons in commercial concessions operated by Landlord, such as gym or athletic facilities, cafes or clubs;
- (p) costs incurred in connection with upgrading the Building to comply with laws, rules, regulations and codes in effect prior to the Lease Commencement Date;
- (q) costs arising from the negligence or willful misconduct of Landlord or other tenants or occupants of the Building or their respective agents, employees, licensees, vendors, contractors or providers of materials or services;
- (r) replacement or contingency reserves;
- (s) the cost of removing or remediating Hazardous Materials from the Property; provided, however, that notwithstanding the foregoing, Operating Expenses shall be permitted to include the costs of remediation or other responses to Hazardous Material first discovered at the Property after the date of this Lease for which a third party or an occupant of the Property other than Landlord or Tenant is responsible and for which Landlord, after using commercially reasonable efforts, has not determined the party that is responsible so that such party can be charged for such costs;
- (s) costs arising from Landlord's charitable or political contributions;
- (t) costs arising from latent defects or repair thereof; and
- (u) costs for sculpture, paintings or other objects of art.

Payments by the Tenant for its share of the Tenant's Operating Expenses Allocable to the Premises shall be made monthly at the time and in the fashion herein provided for the payment of Annual Fixed Rent. The amount so to be paid to the Landlord shall be an amount from time to time reasonably estimated by the Landlord to be sufficient to aggregate a sum equal to the Tenant's share of the Tenant's Operating Expenses Allocable to the Premises for each Operating Fiscal Year.

Not later than one hundred twenty (120) days after the end of each Operating Fiscal Year or fraction thereof during the Term or fraction thereof at the end of the Term, the Landlord shall render the Tenant a statement in reasonable detail and according to usual accounting practices certified by an officer of the Landlord, showing for the preceding Operating Fiscal Year or fraction thereof, as the case may be, the Operating Expenses for the Property and Tenant's Operating Expenses Allocable to the Premises. Said statement to be rendered to the Tenant also shall show for the preceding Operating Fiscal Year or fraction thereof, as the case may be, the amounts of Operating Expenses already paid by the Tenant. If at the time such statement is rendered it is determined with respect to any Operating Fiscal Year, that the Tenant has paid (i) less than the entirety of the Tenant's Operating Expenses

Allocable to the Premises or (ii) more than the Tenant's Operating Expenses Allocable to the Premises, then, in the case of (i) the Tenant shall pay to the Landlord, as Additional Rent, within thirty (30) days of such statement the amounts of such underpayment and, in the case of (ii) the Landlord shall credit the amount of such overpayment against the monthly installments of the Tenant's Operating Expenses Allocable to the Premises next thereafter coming due (or refund such overpayment within thirty (30) days if the Term has expired to the extent that such overpayment exceeds any amount then due from the Tenant to the Landlord). If the Commencement Date occurs on other than the first day of an Operating Fiscal Year, or if the Termination Date occurs on other than the last day of an Operating Fiscal Year, then the amount of Tenant's Operating Expenses Allocable to the Premises payable by the Tenant with respect to such Operating Fiscal Year(s) shall be prorated based upon the ratio of the length of the time period during such Operating Fiscal Year(s) in respect of which the Tenant has an obligation to pay Tenant's Operating Expenses Allocable to the Premises to the length of such Operating Fiscal Year.

The Tenant may examine or audit the accounts and original bills for Operating Expenses upon thirty (30) days' prior written notice to the Landlord, but no more often than one (1) time in any Operating Fiscal Year or Fiscal Year, as applicable. The Landlord agrees that it will make available to the Tenant in the Landlord's office in University Park, during regular business hours, such information as the Landlord has available at such office. In similar manner, the Tenant may examine such further records as Landlord may have, but such matters will be conducted where the Landlord customarily keeps such records, which may be at the headquarters of the Landlord's parent company in Cleveland, Ohio. The Tenant shall bear the cost of any such audit, unless the same discloses a discrepancy in excess of five percent (5%) of the Tenant's Operating Expenses for the Fiscal Year in question, in which event the Landlord shall reimburse the Tenant for such costs reasonably incurred. For any given Fiscal Year of the Landlord, the Tenant must make any such audit within six (6) months after the Tenant's receipt of itemized statements (and any supporting documentation requested by the Tenant) referred to in the preceding paragraph. The Tenant must further make any claim for revision of Operating Expenses for such Fiscal Year by written notice to the Landlord within said six (6) month period. The Tenant shall have the right to deduct from future installments of Operating Expenses any overpayments for Operating Expenses made by Tenant which are disclosed by an audit conducted pursuant to this Section 3.3.

Section 3.4 Utility Charges.

During the Term, the Tenant shall pay directly to the provider of the service, all charges for steam, gas, electricity, fuel, water, sewer and other services and utilities furnished to the Premises and separately metered. Tenant shall purchase electricity from the utility service providing electricity to the Building from time to time. Landlord shall have the right at any time and from time to time to change the electricity provider to the Building. If at any time during the Term, any utility service to the Premises is not separately metered and paid directly to the service provider by Tenant, Tenant's usage and billing shall depend upon Landlord's reading of the check meters (or, if not check metered, upon the reasonable estimate of Tenant's usage as determined by Landlord's engineer) for such service or if, Tenant's usage is non-determinable, based on the proportion of Tenant's rentable square footage compared to other tenants having use of the same utility service. Unless separately metered and paid directly by Tenant, Additional Rent for utilities in the Premises may be estimated monthly by Landlord, based upon the estimate set forth in the preceding sentence, and shall be paid monthly by Tenant as billed with a final accounting based upon actual bills following the conclusion of each Operating Fiscal Year.

Section 3.5 Above Standard Services.

If the Tenant requests and the Landlord elects to provide any services to the Tenant in addition to those described in Exhibit E, the Tenant shall pay to the Landlord, as Additional Rent, the amount billed by Landlord for such services at Landlord's standard rates as from time to time in effect. The cost of such services shall not be deemed to be Operating Expenses for the Property as described in Section 3.3. If the Tenant has requested that such services be provided on a regular basis, the Tenant shall, if requested by the Landlord, pay for such services at their actual cost to Landlord, including, without limitation, a reasonable overhead component, at the time and in the fashion in which Annual Fixed Rent under this Lease is payable. Otherwise, the Tenant shall pay for such additional services within thirty (30) days after receipt of an invoice from the Landlord.

Section 3.6 No Offsets.

Annual Fixed Rent and Additional Rent shall be paid by the Tenant without offset, abatement or deduction except as provided herein. Without limiting the foregoing, Tenant's obligation to pay rent shall be absolute, unconditional, and independent and shall not be discharged or otherwise affected by any law or regulation now or hereafter applicable to the Premises, or any other restriction on Tenant's use, or, except as provided in Article 8, any casualty or taking, or any failure by Landlord to perform or other occurrence; except as expressly set forth in this Lease, Tenant waives all rights now or hereafter existing to terminate, quit or surrender this Lease or the Premises or any part thereof, or to assert any defense in the nature of constructive eviction to any action seeking to recover rent. Nothing in this Section 3.6 shall be deemed to prohibit Tenant from bringing a claim for injunctive relief against Landlord or seeking monetary damages in a separate proceeding against Landlord.

ARTICLE 4

ALTERATIONS

Section 4.1 Consent Required for Tenant's Alterations.

The Tenant shall not make alterations or additions to the Premises except in accordance with complete, coordinated construction plans and specifications therefor first approved by the Landlord, which approval shall not be unreasonably withheld or delayed. There will be no charge for Landlord's review of Tenant's plans, specifications and construction, except for Landlord's reasonable, third party, out-of-pocket expenses. Notwithstanding the foregoing, the Tenant may, from time to time without the Landlord's prior consent and at the Tenant's own expense, make interior non-structural alterations and changes in and to the Premises, provided that such alterations or changes (i) do not diminish the value of the Building, (ii) do not exceed the applicable floor loading capacity of the Building; (iii) do not affect existing mechanical or electrical, plumbing, HVAC or other systems in the Building (except for standard balancing adjustments of existing systems that may be required when adding offices, conference rooms and the like), and/or (iv) do not affect the exterior appearance of the Building (including without limitation by changing glass or making changes to the Premises that are visible from the exterior of the Building), provided that any proposed alterations and changes costing Fifty Thousand

Dollars (\$50,000) or more, and any proposed alterations and changes that do not fulfill the conditions of any of clauses (i) through (iv) above, shall require Landlord's prior approval as aforesaid. Whether or not the Tenant's changes and/or alterations require the Landlord's consent pursuant to this paragraph, the Tenant shall, in each instance, give reasonable prior notice to the Landlord of the presence of Tenant's contractors in the Building and any alterations and changes in and to the Premises which the Tenant intends to undertake, together with a reasonable description of the proposed work and such plans and specifications as the Tenant has therefor. The Landlord shall not be deemed unreasonable for withholding approval of any alterations or additions which (i) would adversely affect any structural or exterior element of the Building, (ii) would adversely affect the general utility of the Building for use by existing tenants or prospective future tenants thereof, (iii) would affect the exterior appearance of the Building in a manner which is not acceptable to the Landlord, in its sole discretion, (iv) will require unusual expense to readapt the Premises to normal use as laboratory space; or (v) would adversely affect existing mechanical or electrical, plumbing, HVAC or other systems in the Building, in each case, with respect to clauses (i)-(v), as reasonably determined by the Landlord in its sole discretion. The Landlord shall not be deemed unreasonable in delaying the approval of any alterations or additions to the extent that Landlord reasonably requires consultation with third party architects or engineers to review the plans for such work. In any notice withholding approval the Landlord shall specify, in reasonable detail, the nature of the Landlord's objection. Neither the Landlord's failure to object to any proposed alterations or additions, nor the Landlord's approval of any plans and specifications furnished by Tenant to Landlord, shall be construed as superseding in any respect, or as a waiver of Landlord's right to enforce, the Tenant's obligation to fulfill all of the terms and conditions of this Lease applicable to any work contemplated thereby. All alterations and additions to the Premises shall be designed in reasonable accordance with the Building design standards promulgated by Landlord from time to time.

Notwithstanding anything to the contrary contained in this Section 4.1, if any of the Tenant's proposed alterations and/or additions affect the roof of the Building, the following additional conditions shall apply:

(a) Such alterations and changes will not in any way interfere with the proper functioning of, and Landlord's access to, equipment located on the roof of the Building or exceed roof loading requirements; and

(b) Adequate measures are taken to reduce the visibility and noise of mechanical equipment, antennae and dishes consistent with the appearance and design scheme required by the Rules and Regulations and any applicable laws, ordinances or regulations of the City of Cambridge.

Promptly following the performance of any alterations or additions to the Premises, the Tenant shall furnish Landlord an "as built" set of plans and specifications for the Premises and a report evidencing the completion of air balancing (to the extent such alterations or additions affected air balancing), in a format reasonably requested by the Landlord.

Section 4.2 Ownership of Alterations and Initial Leasehold Improvements.

All alterations and additions and the Initial Leasehold Improvements shall be part of the Building and owned by the Landlord; provided, however, that the Landlord may require the Tenant to remove certain specialized alterations and additions and Initial Leasehold Improvements at the expiration, or the early termination of this Lease. Landlord shall specify such items at the time of its approval of their installation. All movable equipment, trade fixtures and furnishings not attached to the Premises shall remain the personal property of the Tenant and shall be removed by the Tenant upon expiration or earlier termination of this Lease. Notwithstanding the foregoing, any and all improvements, specifically including movable case work, lab benches, hoods and equipment, funded by the Leasehold Improvements Allowance shall be part of the Building and owned by the Landlord.

Any alterations and additions, if required to be removed upon the termination or expiration of this Lease as hereinabove provided, shall be removed by the Tenant with reasonable care and diligence, including the capping off of all utility connections behind the adjacent interior finish, and the restoration of such interior finish to the extent necessary so that the Premises are left with complete wall, ceiling and floor finishes.

Section 4.3 Construction Requirements for Alterations.

All construction work performed by or on behalf of the Tenant ("Tenant's Work") shall be done in a good and workmanlike manner employing only first class materials and in compliance with the Rules and Regulations (as defined in Section 6.3) that apply to construction, and with all applicable laws and all lawful ordinances, regulations and orders of governmental authority and insurers of the Building. The Landlord or Landlord's authorized agent may (but without any implied obligation to do so) inspect the work of the Tenant at reasonable times and shall give notice of observed defects. Tenant's Work and the installation of furnishings shall always be coordinated in such manner as to maintain harmonious labor relations on the Property and not to damage the Building or interfere with Building construction or operation. Tenant's Work shall be performed by contractors or workmen first approved by the Landlord, which approval the Landlord agrees not to unreasonably withhold or delay. The Tenant, before starting any work, shall receive and comply with the Construction Rules and Regulations attached hereto as Exhibit G and shall (i) cause the Tenant's contractors to comply therewith; (ii) obtain "builder's risk" coverage (in an amount that is reasonable given the quality and quantity of the work to be undertaken) to enhance the insurance coverage otherwise required to be carried by the Tenant hereunder; (iii) secure all licenses and permits necessary for such work; (iv) deliver to the Landlord a statement of the names of its general contractor (or construction manager) and subcontractors who are to perform electrical or plumbing work or are otherwise to perform work that will affect the structure or base building systems of the Building, and the estimated cost to design and construct any Tenant's Work; (v) provide security satisfactory to the Landlord in its reasonable discretion and consistent with the security requirements for comparable work in comparable buildings in the Cambridge market protecting the Landlord against liens arising out of the furnishing of such labor and material; and (vi) cause each contractor to carry worker's compensation insurance in statutory amounts covering all the contractors' and subcontractors' employees and commercial general liability insurance on an occurrence basis with limits of \$1,000,000 (individual) and \$5,000,000 (occurrence) covering personal injury and death and property damage (all such insurance to be written in companies approved reasonably by the Landlord and insuring the Landlord, such individuals and entities affiliated with the Landlord as

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the Landlord may designate, any ground lessor or mortgagee that the Landlord may designate, and the Tenant as well as the contractors and to contain a requirement for at least thirty (30) days' notice to the Landlord prior to cancellation, nonrenewal or material change), and deliver to the Landlord certificates of all such insurance prior to the commencement of the applicable Tenant's Work. Tenant shall reimburse the Landlord within 30 days after invoice for any reasonable third-party expenses incurred by the Landlord in connection with any request by the Tenant for consent to any alterations or additions pursuant to this Article 4.

Section 4.4 Payment for Tenant Alterations.

Except as set forth in the Work Letter, the Tenant agrees to pay promptly when due the entire cost of any work done on the Premises by the Tenant, its agents, employees or independent contractors, and not to cause or permit any liens or notice of intent to file a lien for labor or materials performed or furnished in connection therewith to attach to the Premises or the Property and promptly to discharge (or bond over in a manner satisfactory to Landlord in its sole discretion) any such liens which may so attach. If any such lien or notice of intent to file a lien shall be filed against the Premises or the Property and the Tenant shall fail to cause such lien or notice to be discharged within fifteen (15) days after receipt by the Tenant of notice of the filing thereof, the Landlord may cause such lien or notice to be discharged by payment or otherwise without investigation as to the validity thereof or as to any offsets or defenses which the Tenant may have with respect to the amount claimed. The Tenant shall reimburse the Landlord, as additional rent, for any cost so incurred and shall indemnify and hold harmless the Landlord from and against any and all claims, costs, damages, liabilities and expenses (including reasonable attorneys' fees) which may be incurred or suffered by the Landlord by reason of any such lien or its discharge.

Section 4.5 Initial Leasehold Improvements.

Tenant shall have the right to perform some initial work to the Premises prior to occupancy (the "Initial Leasehold Improvements"). The construction of the Initial Leasehold Improvements shall be done in accordance with the terms of this Section 4 and the work letter attached hereto as Exhibit E-1 (the "Work Letter"). Additionally, and subject to the terms set forth herein and in the Work Letter, Tenant may hire its own architect and engineer for the construction of the Initial Leasehold Improvements, subject to the approval of the Landlord, which shall not be unreasonably withheld. There shall be no construction oversight fee paid to Landlord. However, Landlord shall be reimbursed for any third party out of pocket costs incurred by Landlord in the review and approval of Tenant's plans, specifications, improvements and construction. Tenant agrees to use The Richmond Group (the "Contractor") as its general contractor for the Initial Leasehold Improvements. As construction of the Landlord's Work and the Initial Leasehold Improvements will be ongoing simultaneously, both Landlord and Tenant agree to use good faith efforts to cooperate with each other to ensure the various construction activities occur without unreasonable conflict.

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ARTICLE 5

RESPONSIBILITY FOR CONDITION OF BUILDING AND PREMISES

Section 5.1 Maintenance of Building and Common Areas by Landlord.

Except as otherwise provided in Article 8, the Landlord shall make such repairs to the foundation, roof, exterior walls (including exterior glass), floor slabs, elevators, base building mechanical, plumbing and electrical and life safety systems (to the extent serving more than one tenant), and any other base structural elements of the Building as may be necessary to keep them in good order, condition and repair, and make such repairs to the mechanical systems and equipment serving the Building, except for any mechanical, plumbing and electrical systems and equipment that serve the Premises exclusively (“Tenant’s Dedicated Mechanical Systems and Equipment”), and other Common Areas as are necessary to keep them in good order, condition and repair. The Landlord shall further perform the services designated as Landlord’s Services on Exhibit E. Landlord shall also provide a dumpster and/or compactor at the loading area of the Building for use by Tenant in common with other tenants for the disposal of non-hazardous and non-controlled substances. Costs and expenses incurred by the Landlord under this Section 5.1 shall be included in Operating Expenses of the Property as permitted under Section 3.3. Subject to Section 7.5, the Tenant shall be responsible for 100% of the cost of any repair to the Premises, the Building, or the Land caused by the negligence or misconduct of the Tenant, or any agent, employee or contractor of the Tenant, notwithstanding anything to the contrary provided in Section 3.3.

Without limiting the foregoing, Landlord shall provide stand-by power by automatic transfer switches and power from the generator installed by Landlord on the roof of the Building, provided that Tenant’s allowance of such power is 4 watts per square foot of the Premises.

Section 5.2 Maintenance of Premises by Tenant.

The Tenant shall keep and maintain in good order, condition and repair the Premises and every part thereof and all of Tenant’s Dedicated Mechanical Systems and Equipment, reasonable wear and tear and damage by fire or other casualty excepted (provided that subject to Section 7.5, the Landlord shall be responsible for damage caused by the fault or neglect of the Landlord, or the Landlord’s agents, employees or contractors), excluding those repairs for which the Landlord is responsible pursuant to Sections 5.1, 8.1 and 8.5. The Tenant shall not permit or commit any damage (waste), and the Tenant shall, subject to Section 7.5, be responsible for the cost of repairs which may be made necessary by reason of damage to the Property caused by the negligence or misconduct of the Tenant, or any of the contractors, employees, or agents of the Tenant. Tenant’s Dedicated Mechanical Systems and Equipment, and all other systems and equipment, shall be maintained in good order, condition and repair consistent with prevailing standards at comparable first class leased laboratory buildings, reasonable wear and tear, damage by fire or other casualty, and subject to Section 7.5, damage caused by the fault or neglect of the Landlord, or the Landlord’s agents, employees, or contractors excepted.

Section 5.3 Delays in Landlord's Services.

The Landlord shall not be liable to the Tenant for any compensation or, except as expressly provided below, reduction of rent by reason of inconvenience or annoyance or for loss of business arising from the necessity of the Landlord or its agents entering the Premises for any purposes authorized in this Lease, or for repairing the Premises or any portion of the Building. In case the Landlord is prevented or delayed from making any repairs, alterations or improvements, or furnishing any services or performing any other covenant or duty to be performed on the Landlord's part, by reason of any External Cause, the Landlord shall not be liable to the Tenant therefor, nor, except as expressly otherwise provided in this Lease, shall the Tenant be entitled to any abatement or reduction of rent by reason thereof, except as provided below, nor shall the same give rise to a claim in the Tenant's favor that such failure constitutes actual or constructive, total or partial, eviction from the Premises.

The Landlord reserves the right to stop any service or utility system the Landlord provides or causes to be provided under this Lease when necessary by reason of accident or emergency or exercise of Landlord's rights pursuant to Section 2.3 hereof (following notice as provided therein), or until necessary repairs have been completed; provided, however, that in each instance of stoppage, the Landlord shall exercise reasonable diligence to eliminate the cause thereof and shall not interfere with Tenant's use and occupancy of the Premises. Except in case of emergency repairs, the Landlord will give the Tenant reasonable advance notice of the contemplated stoppage and will use reasonable efforts to avoid unnecessary inconvenience to the Tenant by reason thereof. To the extent that the Landlord is providing or causing to be provided heat, light or any utility or service, in no event shall the Landlord have any liability to the Tenant for the unavailability of the same to the extent that such unavailability is caused by External Causes, provided, however, that the Landlord is obligated to exercise reasonable efforts to restore such services or utility systems' operation. The Landlord agrees to carry rent interruption insurance in commercially reasonable amounts which permits recovery within, to the extent reasonably available, five (5) days after the insured peril, provided however that the failure by Landlord to carry such rent interruption insurance shall not affect Tenant's rights hereunder.

If the unavailability of heat, light or any utility or service provided or caused to be provided by the Landlord, other than the unavailability of the same due to the Tenant's acts or omissions, renders all or any portion of the Premises untenantable for the Tenant's use as permitted under this Lease, and the Tenant ceases to occupy the same for the conduct of its business, the Tenant shall receive an equitable abatement of rent, taking into account the extent of the Tenant's loss of use of the Premises as the result thereof, beginning on and after the third (3rd) business day following the commencement of such condition of untenantability. For all purposes of this Lease, if Tenant has responsibility for maintenance and repair of any aspect of the Building or any equipment or system therein, the functioning and performance of the same shall be the responsibility of the Tenant under this Lease, and shall in no event constitute a service or utility system that the Landlord provides or causes to be provided under this Lease.

Section 5.4 Tenant's Responsibilities Regarding Hazardous Materials.

The Tenant covenants and agrees that the Tenant shall not use, generate, store or dispose, nor shall the Tenant suffer or permit the use, generation, storing or disposal in the Premises or otherwise by any of Tenant's contractors, licensees, invitees, agents or employees, of any oil, toxic substances, hazardous wastes or hazardous materials (collectively, "Hazardous Materials")

in, on or about the Premises, the Building or the Land, except for Hazardous Materials that are necessary and customary for Tenant's operation of Tenant's Permitted Use (which Permitted Use is set forth on Exhibit A), and in all cases such Hazardous Materials must be used, generated, stored and disposed of by Tenant in compliance with all applicable law and regulations. The Tenant covenants and agrees that the Tenant shall comply with all applicable laws and regulations in handling and disposing of materials used in its research and other uses of the Premises, whether or not considered Hazardous Materials, and Tenant shall not dump, flush or cause the other introduction of Hazardous Materials or such other inappropriate materials into the septic, sewage or other waste disposal systems serving the Premises, except as specifically permitted by law or regulation and subject to the conditions and qualifications imposed by any governmental license or permit. The Tenant covenants and agrees that the Tenant shall, at its sole cost, promptly remove or remediate all Hazardous Materials that are found upon the Premises, the Building or the Land by virtue of the failure of the foregoing covenants and agreements to have been fulfilled, or otherwise as the result of the act or omission of Tenant or its contractors, licensees, agents or employees, in a manner complying with all applicable laws and regulations and the provisions of this Lease. If the Tenant should have any responsibility under this Section 5.4 to remove or remediate Hazardous Materials, the Tenant shall keep the Landlord reasonably informed as to the status of the environmental condition at issue, promptly furnish to the Landlord copies of all regulatory filings with any governmental regulatory agencies in connection therewith, and substantiate the performance of its obligations under this Section 5.4. At the expiration or earlier termination of the Term, the Tenant shall promptly remove or remediate any Hazardous Materials from the Premises in a manner consistent with accepted "best practices" and in compliance with all legal requirements relating to the closure of laboratory facilities and disposal of equipment and supplies therein.

If Tenant's transportation, storage or use of Hazardous Materials on the Premises results in the release onto or other contamination of any portion of the Property or adjacent areas, including building or parking areas, soil or surface or ground water, or loss or damage to person(s) or property, without limitation, Tenant agrees to: (a) notify Landlord immediately of any release, threat of release, contamination, claim of contamination, loss or damage and (b) after consultation with Landlord, clean up the release, threat of release, or contamination as required by all applicable statutes, regulations and standards. In the event of such contamination, Tenant agrees to cooperate with Landlord, as Landlord may reasonably request, and provide such documents, affidavits and information as may be reasonably requested by Landlord (1) to comply with any applicable laws, and/or (2) for any other reason deemed necessary by Landlord in its reasonable discretion. Tenant shall notify Landlord promptly in the event of any spill or other release of any Hazardous Materials at, in, on, under or about the Premises that is required to be reported to a governmental authority under any applicable laws, shall promptly forward to Landlord copies of any notices received by Tenant relating to alleged violations of any applicable laws and shall promptly pay when due any fine or assessment against Landlord, Tenant, or the Premises relating to any violation during the Term of any applicable laws by Tenant, its employees, agents, or independent contractors, or with respect to the Premises or the remainder of the Property. If any governmental authority files a lien against the Premises or the remainder of the Property due to any act or omission, intentional or unintentional, of Tenant, its agents, or employees, or for which Tenant is responsible, resulting in the releasing, spilling, leaking, leaching, pumping, emitting, pouring, emptying or dumping of any Hazardous Materials, Tenant shall, within fifteen (15) days from the date that Tenant is first given notice of

such lien (or within such shorter period of time as may be specified by Landlord if such governmental authority takes steps to cause the Premises to be sold pursuant to such lien) either (A) pay the claim and remove the lien or (B) furnish a cash deposit, bond or such other security as is reasonably satisfactory in all respects to Landlord and sufficient to discharge the lien completely. Tenant shall defend, indemnify Landlord and hold Landlord harmless from and against any damages, liability or expense associated with claims by governmental or other third parties arising out of the presence, removal or remediation of Hazardous Materials for which Tenant is responsible for removal or remediation under this Section 5.4.

Notwithstanding any provision hereof to the contrary, Tenant shall not be responsible for, and the indemnification and hold harmless obligations set forth in this Section shall not include matters arising from: (A) the existing environmental condition of the Premises or Property as of the Lease Commencement Date or any earlier date of entry into the Premises by Tenant, or (B) Hazardous Materials brought upon, kept, used, stored, handled, treated, generated in or about, or released or disposed of from the Premises during the Term by Landlord or by another tenant or occupant of the Building or any of their respective officers, directors, employees, agents or contractors.

Section 5.5 Landlord's Responsibilities Regarding Hazardous Materials.

Landlord has provided Tenant with a copy of the decommissioning report(s) for the Premises. During the Term of this Lease, if the removal or remediation of Hazardous Materials from the Premises, Building or Land is required to be undertaken, then except to the extent such obligation is the responsibility of the Tenant under Section 5.4 hereof, the Landlord covenants and agrees to undertake the same without charge to the Tenant. Without limitation of the foregoing, if necessary to comply with any applicable legal requirements, should any existing environmental condition of the Land require the removal or remediation of Hazardous Materials, the Landlord shall perform such removal or remediation, without charge to the Tenant, when and if required by applicable legal requirements. The Landlord shall keep the Tenant reasonably informed as to the status of the environmental condition at issue, promptly furnish to the Tenant copies of all regulatory filings with any governmental regulatory agencies in connection therewith, and substantiate the performance of its obligations under this Section 5.5.

ARTICLE 6

TENANT COVENANTS

The Tenant covenants during the Term and for such further time as the Tenant occupies any part of the Premises:

Section 6.1 Permitted Uses.

The Tenant shall occupy the Premises only for the Permitted Uses, and shall not injure or deface the Premises or the Property, nor permit in the Premises any auction sale. The Tenant shall not permit in the Premises any nuisance, or the emission from the Premises of any reasonably objectionable noise, odor or vibration, nor use or devote the Premises or any part

thereof for any purpose which is contrary to law or ordinance, or liable to invalidate or increase premiums (above those normally incurred for the Permitted Uses) for any insurance on the Building or its contents (unless the Tenant pays for any such increase in premiums and provided such actions do not interfere with the use and enjoyment of the Land by the Landlord, other tenants, visitors or invitees of the Building) or liable to render necessary any alteration or addition to the Building, nor commit or permit any waste in or with respect to the Premises, nor shall Tenant overload existing electrical or other Building systems.

Section 6.2 Laws and Regulations.

The Tenant shall comply with all federal, state and local laws, regulations, ordinances, executive orders, guidelines, policies and similar requirements in effect from time to time, including, without limitation, all such requirements relating to Tenant's occupancy and use of the Premises and Hazardous Materials. Tenant shall also conform to recognized "best practices" standards with respect to the physical aspects of its operations carried on within the Premises. Tenant shall have the right to contest any notice of violation for any of the foregoing by appropriate proceedings diligently conducted in good faith. Notwithstanding the foregoing or any other provision of this Lease, however, Tenant shall not be responsible for compliance with any such laws, regulations, or the like requiring (a) structural repairs or modifications to the Building; or (b) repairs or modifications to the utility or building service equipment serving the Building (rather than equipment installed by Tenant serving only the Premises); or (c) installation of new building service equipment, such as fire detection or suppression equipment, unless such repairs, modifications, or installations shall (i) be due to Tenant's particular manner of use of the Premises (as opposed to laboratory use generally), or (ii) be due to the negligence or willful misconduct of Tenant or any agent, employee, or contractor of Tenant.

Section 6.3 Rules and Regulations.

The Tenant agrees to comply with the Rules and Regulations set forth in Exhibit F and such other reasonable and non discriminatorily enforced rules and regulations of general applicability ("Rules and Regulations") as (i) may from time to time be made by the Landlord of which the Tenant is given written advanced notice, so far as the same relate to the use of the Building, the Land and the Tenant's appurtenant parking privileges and (ii) may from time to time be promulgated with respect to all or any portion of the Building (including without limitation pursuant to the Declaration of Covenants). The Tenant shall not obstruct in any manner any portion of the Property; and, except as set forth in this Lease, shall not permit the placing of any signs, awnings or flagpoles, or the like, visible from outside the Building. Neither shall Tenant place curtains, blinds or shades or similar window treatments visible from outside the Building in the Premises, except as may be otherwise approved by Landlord.

Section 6.4 Safety Compliance.

The Tenant shall keep the Premises equipped with all safety appliances required by law or ordinance or any other regulations of any public authority because of the manner of use made by the Tenant and to procure all licenses and permits so required because of such manner of use and, if requested by the Landlord, do any work so required because of such use, it being

understood that the foregoing provisions shall not be construed to broaden in any way the Tenant's Permitted Uses.

Section 6.5 Landlord's Entry.

The Tenant shall permit the Landlord and its agents, after at least twenty four (24) hours' notice except in the case of emergencies, to enter the Premises at all reasonable hours for the purpose of inspecting or making repairs to the same, monitoring Tenant's compliance with the requirements and restrictions set forth in this Lease, and for the purpose of showing the Premises to prospective purchasers and mortgagees at all reasonable times and to prospective tenants within twelve (12) months of the end of the Term provided that in connection with such entry, Tenant may provide procedures reasonably designed so as not to jeopardize Tenant's trade secrets, proprietary technology or critical business operations, including accompaniment of all such persons by an employee of the Tenant. In case of an emergency, the Landlord shall make good faith efforts to notify the Tenant in person or by telephone prior to such entry, and in any event, the Landlord shall notify Tenant promptly thereafter such entry.

Section 6.6 Floor Load.

The Tenant shall not place a load upon any floor in the Premises exceeding the floor load per square foot of area (as set forth on Exhibit A) which such floor was designed to carry, which floor load is **[TO BE CONFIRMED: one hundred (100) pounds]** per square foot of area as of the date of this Lease, and which is allowed by law. The Tenant's machines and mechanical equipment shall be placed and maintained by the Tenant at the Tenant's expense in settings sufficient to absorb or prevent vibration or noise that may be transmitted to the Building structure.

Section 6.7 Personal Property Tax.

The Tenant shall pay promptly when due all taxes which may be imposed upon personal property (including, without limitation, fixtures and equipment) in the Premises to whomever assessed. Tenant shall have the right to contest the validity or amount of any such taxes by appropriate proceedings diligently conducted in good faith.

Section 6.8 Assignment and Subleases.

Except as otherwise provided in this Section 6.8, the Tenant shall not assign this Lease or sublet (which term, without limitation, shall include granting of concessions, licenses and the like) the whole or any part of the Premises, nor permit the further underletting or assignment of any sublease or other occupancy agreement (each a "Transfer") without, in each instance, having first received the consent of the Landlord which consent shall not be unreasonably withheld or delayed. Any purported Transfer made without such consent or otherwise not fulfilling the conditions and requirements of this Section 6.8 shall be void, and except as specifically permitted in this Section 6.8, in no event shall the Tenant or anyone claiming by, through or under the Tenant have the right to mortgage, pledge, hypothecate or otherwise transfer this Lease. The Landlord shall not be deemed to be unreasonable in withholding its consent to any proposed Transfer that is subject to the Landlord's consent based on any of the following factors:

(a) If the manner in which the proposed occupant conducts its business operations is not consistent, in Landlord's reasonable opinion, with the image and character of the Park development as a first-class biotechnology office/research and development park, then the withholding of consent by the Landlord shall be considered reasonable; and

(b) If the proposed Transfer is (i) an assignment of this Lease, or (ii) a sublease, then in either of such cases, if the proposed occupant is not sufficiently creditworthy and trustworthy in the reasonable opinion of the Landlord with reference to the monetary and other obligations which are to be fulfilled by the Tenant under this Lease, and the reasonable needs of the Landlord to protect the value of the Building, then the withholding of consent by the Landlord shall be considered reasonable.

(c) If the proposed assignee or subtenant is already actively involved in discussions with either the Landlord or any affiliate of the Landlord regarding space within the Park that is or is to become available for lease, then the withholding of consent by the Landlord shall be considered reasonable.

Notwithstanding anything to the contrary contained in this Section, Tenant shall have the right to assign or otherwise Transfer this Lease or the Premises, or part of the Premises, without obtaining the prior consent of Landlord, (a) to its parent entity or to a wholly owned subsidiary or to an entity which is wholly owned by the same entity which wholly owns Tenant or to an entity that controls, is controlled by or under common control with Tenant, where control is the right to direct voting of more than 50% of the ownership interests in the applicable entity (an "Affiliate"), provided that (i) the transferee shall, prior to the effective date of the transfer, deliver to Landlord instruments evidencing such transfer and its agreement to assume and be bound by all the terms, conditions and covenants of this Lease to be performed by Tenant, all in form reasonably acceptable to Landlord and (ii) at the time of such transfer there shall not be an uncured Event of Default under this Lease except in connection with a bona fide dispute that the parties are negotiating in good faith to resolve; or (b) to the purchaser of all or substantially all of its assets or ownership interests in Tenant, or to any entity into which the Tenant may be merged or consolidated (along with all or substantially all of its assets or ownership interests) (the "Acquiring Company"), provided that (i) the net assets of the Acquiring Company at the time of the transfer or merger shall not be less than the net assets of Tenant at the time of the transfer, (ii) the Acquiring Company's use of the Premises shall be consistent with the Permitted Uses described in Exhibit A, (iii) the Acquiring Company shall assume in writing, in form reasonably acceptable to Landlord, all of Tenant's obligations under this Lease, (iv) Tenant shall provide to Landlord such additional information regarding the Acquiring Company as Landlord shall reasonably request, and (v) Tenant shall pay Landlord's reasonable third-party expenses incurred in connection therewith. The transfers described in this paragraph are hereinafter referred to as "Permitted Transfers." Upon request of Tenant, Landlord agrees to execute a reasonable confidentiality agreement prior to Tenant's being required to deliver financial and other information on the assignee or subtenant.

Whether or not the Landlord consents, or is required to consent, to any Transfer, the Tenant named herein shall remain fully and primarily liable for the obligations of the Tenant hereunder, including, without limitation, the obligation to pay Annual Fixed Rent and Additional Rent provided under this Lease.

The Tenant shall give the Landlord at least 30 days prior written notice of any proposed Transfer, specifying the provisions thereof, including (i) the name and address of the proposed occupant, subtenant, assignee or other transferee, (ii) a copy of the proposed occupant's, subtenant's, assignee's, or other transferee's most recent annual financial statement, and (iii) all of the terms and provisions upon which the proposed Transfer is to be made including, without limitation, all of the documentation effectuating such Transfer (which shall be subject to the Landlord's approval not to be unreasonably withheld) and such other reasonable information concerning the proposed Transfer or concerning the proposed occupant, subtenant, assignee or other transferee as the Tenant has obtained in connection with the proposed Transfer. The Tenant shall reimburse the Landlord promptly for reasonable legal and other reasonable expenses incurred by the Landlord in connection with any request by the Tenant for consent to any Transfer. If this Lease is assigned, or if the Premises or any part thereof is sublet or occupied by anyone other than the Tenant, or there is otherwise a Transfer, then during any time when an Event of Default is subsisting, the Landlord may, at any time and from time to time, collect rent and other charges from the assignee, sublessee, occupant or transferee, and apply the net amount collected to the rent and other charges herein reserved, but no such assignment, subletting, occupancy or collection shall be deemed a waiver of the prohibitions contained in this Section 6.8 or the acceptance of the assignee, sublessee or occupant as a tenant or a release of the Tenant from the further performance by the Tenant of covenants on the part of the Tenant herein contained.

Except for Transfers to an Affiliate or an Acquiring Company, the Tenant shall pay to the Landlord fifty percent (50%) of any amounts the Tenant receives from any occupant, subtenant, assignee or other transferee as rent, additional rent or other forms of compensation or reimbursement (if any) in excess of the aggregate amount of (i) the proportionate monthly share of Annual Fixed Rent, Additional Rent and all other monies due to Landlord pursuant to this Lease (allocable in the case of a sublease to that portion of the Premises being subleased), (ii) all costs associated with assigning or subleasing the Premises or any portion of the Premises, including without limitation, rent concessions, brokerage commissions and reasonable fees for legal services associated with the transaction, (iii) Tenant's costs to prepare the space for the assignee or subtenant ("Sublease Transaction Expenses"), (iv) the costs of Tenant's leasehold improvement in excess of the LIA, and (v) consideration payable to Tenant other than for the transfer of the interest in the leasehold estate hereunder, such as charges for use of shared equipment and services to be provided by Tenant to such transferee. In the circumstances where the transferee pays the consideration due to the Tenant on account of such transfer over time (e.g. monthly rental payments under a sublease), Sublease Transaction Expenses referred to in clauses (ii), (iii) and (iv) of the preceding sentence shall be amortized on a straight line basis over the term of the transfer in question. The consent by the Landlord to a Transfer for which the Landlord's consent is required shall not be construed to relieve the Tenant from the obligation to obtain the express consent in writing of the Landlord to any further Transfer whether by the Tenant or by anyone claiming by, through or under the Tenant including, without limitation, any occupant, assignee, subtenant or other transferee.

Except for Transfers to an Affiliate if the portion of the Premises that is subject to the proposed assignment or subletting is larger than 25% of the Premises and the proposed assignment or subletting is for the duration of the then remaining Term, then the Landlord may elect, within thirty (30) days of receipt of written notice from the Tenant of any proposed

assignment or sublease of all or any portion of the Premises prior to approving or disapproving any such proposed assignment or sublease, to repossess the Premises or the portion of the Premises under consideration. The Landlord may thereafter lease the Premises in such a manner as the Landlord may in its sole discretion determine. In the event the Landlord elects to repossess the Premises or the portion of the Premises under consideration as provided above, then all of the Tenant's rights and obligations hereunder with respect to the Premises shall cease and shall be of no further force and effect.

ARTICLE 7

INDEMNITY AND INSURANCE

Section 7.1 Indemnity.

To the maximum extent this agreement may be made effective according to law, the Tenant agrees to defend, indemnify and save harmless the Landlord from and against all claims, loss, or damage of whatever nature arising from any breach by Tenant of any obligation of Tenant under this Lease beyond applicable notice and cure periods or from any act, omission or negligence of the Tenant, or the Tenant's contractors, licensees, invitees, agents, servants or employees, or arising from any accident, injury or damage whatsoever caused to any person or property, occurring after the date that possession of the Premises is first delivered to the Tenant and until the end of the Term and thereafter, so long as the Tenant is in occupancy of any part of the Premises, in or about the Premises or arising from any accident, injury or damage occurring outside the Premises but within the Building, on the Land, on the access roads and ways, in the parking facilities provided pursuant to the Lease, within University Park or any adjacent area maintained by Landlord or any individual or entity affiliated with Landlord, where such accident, injury or damage results from a negligent act or omission or willful misconduct on the part of the Tenant or the Tenant's agents or employees, licensees, invitees, servants or contractors, provided that the foregoing indemnity shall not include any cost or damage to the extent arising from any act, omission or negligence of the Landlord, or the Landlord's contractors, licensees, invitees, agents, servants or employees.

Landlord agrees to defend, indemnify and save harmless Tenant from legal action, damages, loss, liability and any other expense in connection with loss of life, bodily or personal injury or property damage, arising from or out of the intentional or willful misconduct or negligence of Landlord, its agents, employees, licensees, servants, invitees or contractors, which occur in or about the Premises, outside the Premises but within the Building, on the Land, on the access roads and ways, in the parking facilities provided pursuant to the Lease, within University Park or any adjacent area maintained by Landlord, except to the extent that such loss of life, bodily or personal injury or property damage is due to the willful misconduct or negligent act, omission or neglect of Tenant, its agents, contractors, employees, licensees, invitees or servants.

The foregoing indemnities and hold harmless agreements shall include indemnity against reasonable attorneys' fees and all other costs, expenses and liabilities incurred in connection with any such claim or proceeding brought thereon, and the defense thereof.

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Section 7.2 Liability Insurance.

The Tenant agrees to maintain in full force from the date upon which the Tenant first enters the Premises for any reason, throughout the Term, and thereafter, so long as the Tenant is in occupancy of any part of the Premises, by a program of self-insurance acceptable to Landlord, or by a policy of commercial general liability insurance under which the Landlord (and the Building's managing agent, any ground lessor and any holder of a first mortgage on the Property of whom the Tenant is notified by the Landlord, collectively, the "Additional Named Insureds") and the Tenant are named as insureds, and under which the insurer provides a contractual liability endorsement insuring against all cost, expense and liability arising out of or based upon any and all claims, accidents, injuries and damages described in Section 7.1, in the broadest form of such coverage from time to time available. Unless provided by self-insurance, each such policy shall be noncancellable and nonamendable (to the extent that any proposed amendment reduces the limits or the scope of the insurance required in this Lease) with respect to the Landlord and such ground lessor and first mortgagee without thirty (30) days' prior notice to the Landlord and the Additional Named Insureds, except for notice of cancellation due to non-payment of premium, if any, which shall be ten (10) days' prior notice, and a certificate of insurance shall be delivered to the Landlord. The minimum limits of liability of such insurance as of the Commencement Date shall be Five Million Dollars (\$5,000,000.00) per occurrence for combined bodily injury (or death) and damage to property.

Notwithstanding anything in this Lease to the contrary, Tenant may elect to self-insure against any and all of the risks, or portion thereof, against which Tenant is required to insure pursuant to the terms of this Lease, provided that either (i) the Chief Financial Officer of Tenant certifies annually that Tenant has a US tax tangible net worth, as of the end of the Tenant's most recent reporting period of not less than One Hundred Fifty Million Dollars (\$150,000,000) as computed in accordance with the Generally Accepted Accounting Principles (GAAP), ("Tenant's Net Worth"), or (ii) the Chief Financial Officer of Guarantor certifies annually that Guarantor has a US tax tangible net worth, as of the end of the Guarantor's most recent reporting period, of not less than One Hundred Fifty Million Dollars (\$150,000,000) as computed in accordance with GAAP, ("Guarantor's Net Worth"). With regard to this Lease, self-insurance will be considered as insurance for the purposes of complying with the terms and conditions of the Lease. Should Tenant's Net Worth be less than \$150 Million, Tenant may not avail itself of the election to self-insure.

Section 7.3 Alterations, Improvements and Betterments; Personal Property at Risk.

The Tenant agrees to maintain in full force at all times throughout the Term, policy(s) of all risk property damage insurance, naming Landlord (and the Additional Named Insureds) and the Tenant as insureds as their interests may appear, or a program of self-insurance acceptable to Landlord, covering all of Tenant's leasehold improvements and alterations to the extent of their full replacement costs as updated from time to time during the Term.

Unless caused by the Landlord or its agents, employees, servants or contractors, the Tenant agrees that all of the furnishings, fixtures, equipment, effects and property of every kind, nature and description of the Tenant and of all persons claiming by, through or under the Tenant which, during the continuance of this Lease or any occupancy of the Premises by the Tenant or anyone claiming under the Tenant which, during the continuance of this Lease or any occupancy of the Premises by the Tenant or anyone claiming under the Tenant, may be on the Premises or elsewhere in the Building

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or on the Land or parking facilities provided hereby, shall be at the sole risk and hazard of the Tenant, and if the whole or any part thereof shall be destroyed or damaged by fire, water or otherwise, or by the leakage or bursting of water pipes, steam pipes, or other pipes, by theft or from any other cause, no part of said loss or damage is to be charged to or be borne by the Landlord, except that the Landlord shall in no event be exonerated from any liability to the Tenant (subject to Section 7.5 hereof) for any injury, loss, damage or liability to the extent same is caused by Landlord's, or its agents', employees', servants' or contractors', negligence or willful misconduct.

Section 7.4 Landlord's Insurance.

The Landlord shall carry, or cause to be carried, such casualty and liability insurance upon and with respect to operations at the Building as may from time to time be deemed reasonably prudent by the Landlord or required by any mortgagee holding a mortgage thereon or any ground lessor of the Land, and in any event, insurance against loss by fire and the risks now covered by extended coverage endorsement No. 4 in an amount at least equal to the full replacement cost of the Building, exclusive of foundations, excavations and footings.

Section 7.5 Waiver of Subrogation.

Any insurance carried by either party, or caused to be carried by either party, with respect to the Building, Land, Premises, parking facilities or any property therein or occurrences thereon shall, without further request by either party, include a clause or endorsement denying to the insurer rights of subrogation against the other party to the extent rights have been waived by the insured prior to occurrence of any claim, damage, injury or loss. Each party, notwithstanding any provisions of this Lease to the contrary, hereby waives any claims or rights of recovery against the other for injury or loss, including, without limitation, injury or loss caused by negligence of such other party to the extent covered by insurance actually carried or required to be carried hereunder.

ARTICLE 8

CASUALTY AND EMINENT DOMAIN

Section 8.1 Restoration Following Casualties.

If, during the Term, the Building or the Premises shall be damaged by fire or casualty, subject to termination rights of the Landlord and the Tenant provided below in this Article 8, the Landlord shall proceed promptly to exercise diligent efforts to restore, or cause to be restored, the Building to substantially the condition thereof just prior to time of such damage, but the Landlord shall not be responsible for delay in such restoration which may result from External Causes. Provided that the Landlord complies with its obligations to carry casualty insurance in accordance with Section 7.4, the Landlord shall have no obligation to expend in the reconstruction of the Building more than the sum of the amount of any deductible and the actual amount of insurance proceeds made available to the Landlord by its insurer, and any additional costs associated with changes to the Premises desired by the Tenant and permitted by Article 4 shall be paid by the Tenant in the manner reasonably required by the Landlord. Any restoration of the Building or the Premises shall be altered to the extent necessary to comply with then current and applicable laws and codes. The Landlord shall, as soon as possible after any

casualty, but in any event no later than sixty (60) days after such casualty, provide to the Tenant a reasonable written estimate (“Contractor’s Estimate”) from a reputable construction or design professional as to the time frame within which the Landlord will be able to repair the casualty damage and the cost of repairing such damage.

Section 8.2 Landlord’s Termination Election.

If the Landlord reasonably determines, based upon the Contractor’s Estimate, that (a) the amount of insurance proceeds available to the Landlord is insufficient to cover the cost of restoring the Building by more than the amount of any deductible, or (b) the Landlord will be unable to restore the Building within twelve (12) months from the date of such casualty, then the Landlord may terminate this Lease by giving notice to the Tenant. Any such termination shall be effective on the date designated in such notice from the Landlord, but in any event not later than sixty (60) days after such notice, and if no date is specified, effective upon the delivery of such notice. Failure by the Landlord to give the Tenant notice of termination within sixty (60) days following the occurrence of the casualty shall constitute the Landlord’s agreement to restore the Building as contemplated in Section 8.1.

Section 8.3 Tenant’s Termination Elections.

If, based upon the Contractor’s Estimate, the time period for repairing any casualty damage will exceed twelve (12) months after the date of any casualty, then the Tenant shall have the right, exercisable by written notice given on or before the date thirty (30) days after the Landlord gives to the Tenant the Contractor’s Estimate, to terminate this Lease.

If neither the Landlord nor the Tenant exercise their termination rights, but the Landlord has failed to restore the Building, within the longer of twelve (12) months from the date of the casualty or taking or the period of restoration set forth in the Contractor’s Estimate set forth in the Contractor’s Estimate, such period to be subject, however, to extension where the delay in completion of such work is due to External Causes, the Tenant shall have the right to terminate this Lease at any time after the expiration of such period (in either case, as extended by delay due to External Causes as aforesaid) until the restoration is substantially completed, such termination to take effect as of the date of the Tenant’s notice. However, if the Landlord has been diligently prosecuting the repair of all casualty and damage, and if the Landlord reasonably determines at any time, and from time to time, during the restoration, based upon certification by its architect or other design professional, that such restoration will not be able to be completed before the deadline date after which the Tenant may terminate this Lease under this Section 8.3, and the Landlord specifies in a notice to Tenant to such effect a later date that the Landlord estimates will be the date upon which such restoration will be completed, then the Tenant may terminate this Lease within thirty (30) days of the Landlord’s notice as aforesaid, failing which the deadline date shall be extended to the date set forth in Landlord’s notice (as extended by delay due to External Causes as aforesaid). The Landlord shall exercise reasonable efforts to keep the Tenant advised of the status of restoration work from time to time, and promptly following any request for information during the course of the performance of the restoration work.

Section 8.4 Casualty at Expiration of Lease.

If the Premises shall be damaged by fire or casualty in such a manner that the Premises cannot, in the ordinary course, reasonably be expected to be repaired within sixty (60) days from the commencement of repair work and such casualty or damage occurs within the last twelve (12) months of the Term (as the same may have been extended prior to such casualty or damage), either party shall have the right, by giving notice to the other not later than sixty (60) days after such casualty or damage, to terminate this Lease, whereupon this Lease shall terminate as of the date of such notice.

Section 8.5 Eminent Domain.

Except as hereinafter provided, if the Premises, or such portion thereof as to render the balance (if reconstructed to the maximum extent practicable in the circumstances) unsuitable for continued occupancy for the purposes contemplated under this Lease, or if access to the Building or Premises, shall be taken by condemnation or right of eminent domain, the Landlord and the Tenant shall each have the right to terminate this Lease by notice to the other of its desire to do so, provided that such notice is given not later than thirty (30) days after receipt by the Tenant of notice of the effective date of such taking. If so much of the Building shall be so taken that the Landlord reasonably determines, in good faith, that it would be necessary to substantially alter the Building so that a rebuilt Building will not be substantially similar to the Building before such taking, the Landlord shall have the right to terminate this Lease by giving notice to the Tenant of the Landlord's desire to do so not later than thirty (30) days after the effective date of such taking.

Should any part of the Premises be so taken or condemned during the Term, and should this Lease be not terminated in accordance with the foregoing provisions, the Landlord agrees to use reasonable efforts to put what may remain of the Premises into proper condition for use and occupation as nearly like the condition of the Premises prior to such taking as shall be practicable, subject, however, to applicable laws and codes then in existence. The Landlord shall have no obligation to expend in the aforesaid restoration more than the proceeds of any award received in any condemnation or eminent domain proceeding, or any sum paid in lieu thereof.

Section 8.6 Rent After Casualty or Taking.

If the Premises shall be damaged by fire or other casualty, until the Lease is terminated or the Premises is restored, the Annual Fixed Rent and Additional Rent shall be justly and equitably abated and reduced according to the nature and extent of the loss of use thereof suffered by the Tenant. In the event of a taking which permanently reduces the area of the Premises, a just proportion of the Annual Fixed Rent and applicable Additional Rent shall be abated for the remainder of the Term.

Section 8.7 Temporary Taking.

In the event of any taking of the Premises or any part thereof for a temporary use not in excess of six (6) months, (i) this Lease shall be and remain unaffected thereby and Annual Fixed Rent and Additional Rent shall not abate, and (ii) the Tenant shall be entitled to receive for itself such portion or portions of any award made for such use with respect to the period of the taking which is within the Term.

Section 8.8 Taking Award.

Except as otherwise provided in Section 8.7, the Landlord shall have and hereby reserves and accepts, and the Tenant hereby grants and assigns to the Landlord, all rights to recover for damages to the Building and the Land, and the leasehold interest hereby created, and to compensation accrued or hereafter to accrue by reason of such taking, damage or destruction, as aforesaid, and by way of confirming the foregoing, the Tenant hereby grants and assigns to the Landlord, all rights to such damages or compensation. Nothing contained herein shall be construed to prevent the Tenant from prosecuting in any condemnation proceedings a separate claim for relocation expenses, Tenant's personal property and any amounts paid by Tenant for the Tenant Improvements in excess of the LIA.

ARTICLE 9

DEFAULT

Section 9.1 Tenant's Default.

Each of the following shall constitute an Event of Default:

- (a) Failure on the part of the Tenant to pay the Annual Fixed Rent, Additional Rent or other charges for which provision is made herein on or before the date on which the same become due and payable, if such condition continues for ten (10) days after written notice that the same are due.
- (b) Failure on the part of the Tenant to perform or observe any other term or condition contained in this Lease if the Tenant shall not cure such failure within thirty (30) days after written notice from the Landlord to the Tenant thereof, provided that in the case of breaches that are not reasonably susceptible to cure within thirty (30) days through the exercise of due diligence, then so long as the Tenant commences such cure within thirty (30) days, and the Tenant diligently pursues such cure to completion, such breach shall not be deemed to create an Event of Default.
- (c) The taking of the estate hereby created on execution or by other process of law against Tenant; or a judicial declaration that the Tenant, or any guarantor of this Lease, is bankrupt or insolvent according to law; or any assignment of the property of the Tenant, or any guarantor of this Lease, for the benefit of creditors; or the appointment of a receiver, guardian, conservator, trustee in bankruptcy or other similar officer to take charge of all or any substantial part of the property of Tenant, or any guarantor of this Lease, by a court of competent jurisdiction, which officer is not dismissed or removed within (60) days; or the filing of an involuntary petition against the Tenant, or any guarantor of this Lease, under any provisions of the bankruptcy act now or hereafter enacted if the same is not dismissed within sixty (60) days; the filing by the Tenant, or any guarantor of this Lease, of any voluntary petition for relief under provisions of any bankruptcy law now or hereafter enacted.

If an Event of Default shall occur, then, in any such case, whether or not the Term shall have begun, Landlord and its agents lawfully may, in addition to any remedies for any preceding

Event of Default and any remedies otherwise available at law or equity, immediately or at any time thereafter without further demand or notice in accordance with process of law, enter upon any part of the Premises in the name of the whole or mail or deliver a notice of termination of the Term of this Lease addressed to Tenant at the Premises or any other address herein, and thereby terminate the Term and repossess the Premises as of Landlord's former estate. At Landlord's election such notice of termination may be included in any notice of default. Upon such entry or mailing the Term shall terminate, all executory rights of Tenant and all obligations of Landlord will immediately cease, and Landlord may expel Tenant and all persons claiming under Tenant and remove their effects without any trespass and without prejudice to any remedies for arrears of rent or prior breach; and Tenant waives all statutory and equitable rights to its leasehold (including rights in the nature of further cure or redemption, if any to the extent such rights may be waived). Subject to Section 9.5, if Landlord engages attorneys in connection with any failure to perform by Tenant hereunder, Tenant shall reimburse Landlord for the reasonable fees of such attorneys on demand as Additional Rent. Without implying that other provisions do not survive, the provisions of this Article shall survive the Term or earlier termination of this Lease.

Section 9.2 Damages.

In the event that this Lease is terminated, the Tenant covenants to pay to the Landlord punctually all the sums ("Periodic Payments") and perform all the obligations which the Tenant covenants in this Lease to pay and to perform in the same manner and to the same extent and at the same time as if this Lease had not been terminated, and all of the Landlord's expenses in connection with reletting the Premises including, without limitation, all repossession costs, brokerage commissions, fees for legal services and expenses of preparing the Premises for such reletting. However, the Landlord may elect, at any time, to demand in lieu of any further obligations to make Periodic Payments, and payments on account of the Landlord's reletting costs thereafter accruing, as compensation, an amount (the "Lump Sum Payment") equal to the excess, if any, of the discounted present value of the total rent reserved for the then remainder of the Term over the then discounted present fair rental value of the Premises for the then remainder of the Term. The discount rate for calculating such sum under the preceding clause (x) shall be the then current rate of United States Treasury securities having a maturity date as close as possible to the end of the Term (had the Lease not been terminated). In calculating the rent reserved, there shall be included, in addition to the Annual Fixed Rent and all Additional Rent, the value of all other considerations agreed to be paid or performed by the Tenant over the remainder of the Term. Should the parties be unable to agree on a fair rental value for the purposes of determining the Lump Sum Payment under clause (x), above, the matter shall be submitted, upon the demand of either party, to the Boston office of the American Arbitration Association, with a request for arbitration in accordance with the rules of the Association by a single arbitrator who shall be real estate broker with at least ten years' experience marketing major office and laboratory projects in the Boston, Massachusetts area. The parties agree that a decision of the arbitrator shall be conclusive and binding upon them.

In calculating the Periodic Payments to be made by the Tenant under the foregoing covenant, the Tenant shall be credited with the net proceeds of any rent obtained by reletting the Premises, after deducting all the Landlord's expenses in connection with such reletting, including, without limitation, all repossession costs, brokerage commissions, fees for legal services and expenses of preparing the Premises for such reletting, provided that Tenant shall

never be entitled to receive any portion of the re-letting proceeds, even if the same exceed the rent originally due hereunder but Tenant shall be credited with such excess amount to offset its obligation to Landlord. The Landlord may (i) relet the Premises, or any part or parts thereof, for a term or terms which may, at the Landlord's option, exceed or be equal to or less than the period which would otherwise have constituted the balance of the Term, and may grant such concessions and free rent as the Landlord in its reasonable commercial judgment considers advisable or necessary to relet the same, (ii) make such alterations, repairs and improvements in the Premises as the Landlord in its reasonable commercial judgment considers advisable or necessary to relet the same, and (iii) any obligation to relet imposed by law shall be subject to the reasonable requirements of Landlord to lease to high quality tenants on such terms (based on then-market standards) as Landlord may from time to time deem appropriate and to develop the Building and Park in a harmonious manner with an appropriate mix of uses, tenants, floor areas and terms of tenancies, and the like, and Landlord shall not be obligated to relet the Premises to any party to whom Landlord or its affiliate may desire to lease other available space in the Park. No action of the Landlord in accordance with foregoing or failure to relet or to collect rent under reletting shall operate to release or reduce the Tenant's liability. The Landlord shall be entitled to seek to rent other properties of the Landlord prior to reletting the Premises without being in breach of any obligation to the Tenant. Landlord agrees to use commercially reasonable efforts to mitigate its damages in the event of a default by Tenant.

Section 9.3 Cumulative Rights.

The specific remedies to which either party may resort under the terms of this Lease are cumulative and, except as expressly set forth herein, are not intended to be exclusive of any other remedies or means of redress to which it may be lawfully entitled in case of any breach or threatened breach by the other party of any provisions of this Lease. In addition to the other remedies provided in this Lease, each party shall be entitled to seek the restraint by injunction of the violation or attempted or threatened violation of any of the covenants, conditions or provisions of this Lease or to a decree compelling specific performance of any such covenants, conditions or provisions. Nothing contained in this Lease shall limit or prejudice the right of the Landlord to prove for and obtain in proceedings for bankruptcy, insolvency or like proceedings by reason of the termination of this Lease, an amount equal to the maximum allowed by any statute or rule of law in effect at the time when, and governing the proceedings in which, the damages are to be proved, whether or not the amount be greater, equal to, or less than the amount of the loss or damages referred to above.

Landlord shall not be required to serve Tenant with any notices or demands as a prerequisite to its exercise of any of its rights or remedies under this Lease, other than those notices and demands specifically required under this Lease. Tenant expressly waives the service of any statutory demand or notice which is a prerequisite to Landlord's commencement of eviction proceedings against Tenant, including the demands and notices specified in any applicable state statute or case law.

Section 9.4 Landlord's Self help.

If there shall be an Event of Default, or if emergency circumstances should exist where, upon the giving of notice or passage of time, such circumstances would constitute an Event of

Default, then the Landlord shall have the right, but not the obligation, after the giving by the Landlord of notice thereof to the Tenant (except in case of emergency circumstances in which case no prior notice need be given), to perform such obligation. In the event the Landlord exercises its rights under this Section 9.4 in case of emergency, the Landlord shall notify the Tenant as soon as reasonably possible after the taking of such action. The Landlord may exercise its rights under this Section without waiving any other of its rights or releasing the Tenant from any of its obligations under this Lease. The Tenant shall be liable to the Landlord for all of the Landlord's reasonable costs associated with effecting such cure.

Section 9.5 Enforcement Expenses; Litigation.

Each party hereto shall promptly reimburse the other for all costs and expenses, including without limitation legal fees, incurred by such party in exercising and enforcing its rights under this Lease following the other party's failure to comply with its obligations hereunder, whether or not such failure constitutes an Event of Default pursuant to Sections 9.1 or 9.7 hereof.

If either party hereto, without fault, is made or becomes a party to any litigation commenced by or against the other party by or against a third party, or incurs costs or expenses related to such litigation, involving any part of the Property and the enforcement of any of the rights, obligations or remedies of such party without fault, then the party becoming involved in any such litigation because of a claim against such other party hereto shall receive from such other party hereto all costs and reasonable attorneys' fees incurred by such party in such litigation. Landlord shall pay all reasonable attorney's fees incurred by Tenant in connection with any legal action concerning an alleged breach of this Lease to the extent that Tenant is the prevailing party. Tenant shall pay all reasonable attorney's fees incurred by Landlord in connection with any legal action concerning an alleged breach of this Lease to the extent that Landlord is the prevailing party.

LANDLORD AND TENANT WAIVE TRIAL BY JURY IN ANY ACTION TO WHICH THEY ARE PARTIES UNDER THIS LEASE.

Section 9.6 Late Charges; Interest on Overdue Payments.

(a) In the event that any payment of Annual Fixed Rent or Additional Rent shall remain unpaid for a period of ten (10) days following notice by the Landlord to the Tenant that such payment is overdue, there shall become due to the Landlord from the Tenant, as Additional Rent and as compensation for the Landlord's extra administrative costs in investigating the circumstances of late rent, a late charge of two percent (2%) of the amount overdue.

(b) Any Annual Fixed Rent and Additional Rent or other amount which is due from either party to the other party which is not paid within ten (10) days after the same is due and payable shall bear interest from the date due until paid at the variable rate (the "Default Interest Rate") equal to the annual rate from time to time announced by Bank of America as its base rate, plus two percent (2%), or if such rate can no longer be determined, the annual prime rate from time to time announced by The Wall Street Journal, plus four percent (4%).

Section 9.7 Landlord's Right to Notice and Cure.

The Landlord shall in no event be in default in the performance of any of the Landlord's obligations hereunder unless and until the Landlord shall have failed to perform such obligations within thirty (30) days, or such additional time as is reasonably required to correct any such default, after written notice by the Tenant to the Landlord expressly specifying wherein the Landlord has failed to perform any such obligation.

ARTICLE 10

MORTGAGEES' RIGHTS

Section 10.1 Subordination.

At the election of the holder of any mortgage (which term for the purpose of this Article shall include a "deed of trust," "ground lease" or similar financing encumbrance) encumbering the Landlord's interest in the Property, this Lease shall be subject and subordinate to the lien of any mortgages thereon, so that the rights of any such mortgagee shall be superior to all rights hereby or hereafter vested in the Tenant, subject however to Section 10.5 hereof, provided, that such mortgagee or ground lessor shall have entered into a subordination non-disturbance and attornment agreement with Tenant. The form of subordination, non-disturbance and attornment agreement ("SNDA") attached hereto as Exhibit is acceptable to Tenant in connection with any mortgage to which this lease shall be subordinated. Landlord shall use commercially reasonable efforts to provide Tenant with agreements in the forms attached to this Lease as Exhibit .

Section 10.2 Attornment; Prepayment of Rent not to Bind Mortgagee.

In the event any holder shall succeed to the interest of Landlord, the Tenant shall, and does hereby agree to attorn to such holder and to recognize such holder as its Landlord and Tenant shall promptly execute and deliver any instrument that such holder may reasonably request to evidence such attornment. Upon such attornment, the holder shall not be: (i) liable in any way to the Tenant for any act or omission, neglect or default on the part of Landlord under this Lease; (ii) subject to any counterclaim or setoff which theretofore accrued to Tenant against Landlord, provided that Tenant shall be entitled to the abatement of rent as provided in Sections 2.1, 2.5, 5.3 and Article 8; (iii) bound by any modification of this Lease subsequent to such mortgage entered into without such holder's consent or by any previous prepayment of regularly scheduled monthly installments of Annual Fixed Rent or more than (1) month, which was not approved in writing by the holder; (iv) liable to the Tenant beyond the holder's interest in the Property; or (v) liable for any portion of a security deposit not actually received by the holder. The covenant and agreement contained in this Lease with respect to the rights, powers and benefits of any such holder constitute a continuing offer to any person, corporation or other entity, which by accepting or requiring an assignment of this Lease or by entry of foreclosure assumes the obligations herein set forth with respect to such holder; every such holder is hereby constituted a party to this Lease and an obligee hereunder to the same extent as though its name was written hereon as such; and such holder shall at its written election be entitled to enforce

such provisions in its own name. No Annual Fixed Rent, Additional Rent (other than estimated monthly payments on account of Additional Rent which the Tenant is required to pay pursuant to the provisions of this Lease), or any other charge payable to the Landlord shall be paid more than thirty (30) days prior to the due date thereof under the terms of this Lease and payments made in violation of this provision shall, except to the extent that such payments are actually received by a mortgagee (which term shall for the purpose of this Lease include a "trustee," "ground lessor" or similar holder of a financing encumbrance) be a nullity as against any of Landlord's mortgagees and the Tenant shall be liable for the amount of such payments to such mortgagee.

Section 10.3 Tenant's Duty to Notify Mortgagee and Mortgagee's Ability to Cure.

The Tenant hereby agrees that, if the Tenant provides the Landlord with any notice of default or claimed default on the part of the Landlord under the Lease, the Tenant shall concurrently therewith send a copy of such notice to the holder of any mortgage of whom the Tenant has been given prior written notice together with its address. In such event, the mortgagee shall be permitted (but not obligated) to cure any such default within the cure period provided to Landlord and any additional period to which such mortgagee shall be entitled pursuant to this Section 10.3. No act or failure to act on the part of the Landlord which would entitle the Tenant under the terms of this Lease, or by law, to be relieved of the Tenant's obligations to pay Annual Fixed Rent or Additional Rent hereunder or to terminate this Lease, shall result in a release or termination of such obligations of the Tenant or a termination of this Lease unless (i) the Tenant shall have first given written notice of the Landlord's act or failure to act to any mortgagee of whom Tenant has been given prior notice, specifying the act or failure to act on the part of the Landlord which would give basis to the Tenant's rights; and (ii) no such mortgagee, after receipt of such notice, shall have corrected or cured the condition complained of within the period provided for Landlord's cure, plus a reasonable period thereafter not to exceed thirty (30) days.

Section 10.4 Estoppel Certificates.

The Tenant shall from time to time, upon not less than ten (10) days' prior written request by the Landlord, execute, acknowledge and deliver to the Landlord a statement in writing certifying to the Landlord or an independent third party, with a true and correct copy of this Lease attached thereto, together with all amendments thereto, to the extent such statements continue to be true and accurate, (i) that this Lease is unmodified and in full force and effect (or, if there have been any modifications, that the same is in full force and effect as modified and stating the modifications); (ii) that the Tenant has no knowledge of any defenses, offsets or counterclaims against its obligations to pay the Annual Fixed Rent and Additional Rent and to perform its other covenants under this Lease (or if there are any defenses, offsets, or counterclaims, setting them forth in reasonable detail); (iii) that there are no known uncured defaults of the Landlord or the Tenant under this Lease (or if there are known defaults, setting them forth in reasonable detail); (iv) the dates to which the Annual Fixed Rent, Additional Rent and other charges have been paid; (v) that the Tenant has accepted, and is in full possession of the Premises, including all improvements, additions and alterations thereto required to be made by Landlord under the Lease (except to the extent stated); (vi) that the Landlord has satisfactorily complied with all of the requirements and conditions precedent to the occurrence of the

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Commencement Date (except to the extent stated); (vii) that the Tenant has been in occupancy since the Commencement Date and paying rent since the specified dates (except to the extent stated); (viii) that no monetary or other considerations, including, but not limited to, rental concessions for Landlord, special tenant improvements or Landlord's assumption of prior lease obligations of Tenant have been granted to Tenant by Landlord for entering into Lease (except as set forth in this Lease or as otherwise specified in such estoppel); (ix) that the Tenant has no notice of a prior assignment, hypothecation, or pledge of rents or of the Lease (except to the extent stated); (x) that the Lease represents the entire agreement between Landlord and Tenant; (xi) that any notice to Tenant may be given it by certified or registered mail, return receipt requested, or delivered, at the Premises, or at another address specified; and (xii) such factual other matters with respect to the Tenant and this Lease as the Landlord may reasonably request. Any statement delivered pursuant to this Section may be relied upon by any prospective purchaser, mortgagee, trustee or ground lessor of the Premises or any interest therein, and shall be binding on the Tenant.

Landlord shall from time to time, upon not less than ten (10) days' prior written request by the Tenant, execute, acknowledge and deliver to the Tenant a statement in writing certifying to the Tenant or an independent third party, with a true and correct copy of this Lease attached thereto, to the extent such statements continue to be true and accurate (i) that this Lease is unmodified and in full force and effect (or, if there have been any modifications, that the same is in full force and effect as modified and stating the modifications); (ii) that the Landlord has no knowledge of any defenses, offsets or counterclaims against its obligations to perform its covenants under this Lease (or if there are any defenses, offsets, or counterclaims, setting them forth in reasonable detail); (iii) that there are no known uncured defaults of the Tenant or the Landlord under this Lease (or if there are known defaults, setting them forth in reasonable detail); (iv) the dates to which the Annual Fixed Rent, Additional Rent and other charges have been paid; (v) that the Tenant is in full possession of the Premises; (vi) that Landlord has no notice of a prior assignment of the Lease or sublease of space therein; (vii) that the Lease represents the entire agreement between Landlord and Tenant; (viii) that any notice to Landlord may be given if by certified or registered mail, return receipt requested, or delivered to the Landlord's address listed on Exhibit A, or at another address specified; and (xii) such other factual matters with respect to the Tenant and this Lease as the Tenant may reasonably request. Any statement delivered pursuant to this Section may be relied upon by any prospective assignee or sublessee of Tenant and shall be binding on the Landlord.

Section 10.5 Assignment of Rents.

With reference to any assignment by the Landlord of the Landlord's interest in this Lease, or the rents payable hereunder, conditional in nature or otherwise, which assignment is made to the holder of a mortgage or a ground lessor on property which includes the Premises, the Tenant agrees;

(a) That the execution thereof by the Landlord, and the acceptance thereof by the holder of such mortgage or ground lessor, shall never be treated as an assumption by such holder or ground lessor of any of the obligations of the Landlord hereunder, unless such holder or ground lessor shall, by notice sent to the Tenant, specifically make such election; and

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(b) That, except as aforesaid, such holder or ground lessor shall be treated as having assumed the Landlord's obligations hereunder only upon foreclosure of such holder's mortgage or the taking of possession of the Property, or, in the case of a ground lessor, the termination of the ground lease.

ARTICLE 11

SECURITY DEPOSIT

(a) Letter of Credit. Upon the execution and delivery of this Lease, Tenant shall deliver to Landlord as security for the performance of the obligations of Tenant hereunder, either a cash deposit or a letter of credit in the Security Deposit amount specified in Exhibit A in accordance with this Section (as renewed, replaced, increased and/or reduced pursuant to this Section, the "Letter of Credit"). If Tenant elects to deliver a Letter of Credit, such Letter of Credit shall be in such form as Landlord may reasonably approve. If there is more than one Letter of Credit so delivered by Tenant, such Letters of Credit shall be collectively hereinafter referred to as the "Letter of Credit". The Letter of Credit (i) shall be irrevocable and shall be issued by a commercial bank reasonably acceptable to Landlord (Landlord acknowledging that Silicon Valley Bank is an acceptable bank), (ii) shall require only the presentation to the issuer of a certificate of the holder of the Letter of Credit stating either (a) that a default has occurred under this Lease after the expiration of any applicable notice and cure period (or stating that transmittal of a default notice is barred by applicable bankruptcy or other law if such is the case), or (b) stating that Tenant has not delivered to Landlord a new Letter of Credit having a commencement date immediately following the expiration of the existing Letter of Credit in accordance with the requirements of the Lease, (iii) shall be payable to Landlord and its successors in interest as the Landlord and shall be freely transferable without cost to any such successor or any lender holding a collateral assignment of Landlord's interest in the Lease, (iv) shall be for an initial term of not less than one year and contain a provision that such term shall be automatically renewed for successive one-year periods unless the issuer shall, at least thirty (30) days prior to the scheduled expiration date, give Landlord written notice of such nonrenewal, and (v) shall otherwise be substantially in the form of the letter of credit attached hereto as Exhibit J. Notwithstanding the foregoing, the term of the Letter of Credit for the final period of the Term shall be for a term ending not earlier than the date forty-five (45) days after the last day of the Term.

If Tenant shall be in default under the Lease, after the expiration of any applicable notice or cure period (or if transmittal of a default or other notice is stayed or barred by applicable bankruptcy or other law), Landlord shall be entitled to draw upon the Letter of Credit to the extent reasonably necessary to cure such default. If, not less than thirty (30) days before the scheduled expiration of the Letter of Credit, Tenant has not delivered to Landlord a new Letter of Credit having a commencement date immediately following the expiration of the existing Letter of Credit in accordance with this Section, Landlord shall also have the right to draw upon the full amount of the Letter of Credit without giving any further notice to Tenant. Landlord may, but shall not be obligated to, apply the amount so drawn to the extent necessary to cure Tenant's default under the Lease. Any funds drawn by Landlord on the Letter of Credit and not applied against amounts due hereunder shall be held by Landlord as a cash security deposit, provided that Landlord shall have

no fiduciary duty with regard to such amounts, shall have the right to commingle such amounts with other funds of Landlord, and shall pay no interest on such amounts. After any application of the Letter of Credit by Landlord in accordance with this paragraph, Tenant shall reinstate the Letter of Credit to the amount then required to be maintained hereunder, within thirty (30) days of demand. Within forty-five (45) days after the expiration or earlier termination of the Term the Letter of Credit and any cash security deposit then being held by Landlord, to the extent not applied, shall be returned to the Tenant provided that no Event of Default is then continuing.

(b) Pledge.

The Landlord may pledge its right and interest in and to the cash deposit or Letter of Credit to any mortgagee or ground lessor and, in order to perfect such pledge, have such cash deposit or Letter of Credit held in escrow by such mortgagee or ground lessee or grant such mortgagee or ground lessee a security interest therein. In connection with any such pledge or grant of security interest by the Landlord to a mortgagee or ground lessee ("Pledgee") of which Tenant receives notice, Tenant covenants and agrees to cooperate as reasonably requested by the Landlord at no additional cost to Tenant, in order to permit the Landlord to implement the same on terms and conditions reasonably required by such Pledgee.

(c) Transfer of Security Deposit.

In the event of a sale or other transfer of the Building or transfer of this Lease, Landlord shall transfer the cash deposit or Letter of Credit to the transferee at no cost to Tenant, and upon the assumption in writing of such transferee of the obligations of Landlord under this Lease, Landlord shall thereupon be released by Tenant from all liability for the return of such security. The provisions hereof shall apply to every transfer or assignment made of the security to such a transferee. Tenant further covenants that it will not voluntarily assign or encumber or attempt to assign or encumber the Letter of Credit or the proceeds thereof, and that neither Landlord nor its successors or assigns shall be bound by any assignment, encumbrance, attempted assignment or attempted encumbrance.

ARTICLE 12

MISCELLANEOUS

Section 12.1 Notice of Lease.

Tenant agrees not to record this Lease or any short form or memorandum hereof but Landlord shall, together with this Lease, execute and deliver to Tenant for recording a Notice of Lease in accordance with statutory requirements. If required by applicable securities laws, Tenant may file with the Securities and Exchange Commission (the "SEC") a copy of this Lease with terms not required to be reported having been redacted.

Section 12.2 Notices.

Whenever any notice, approval, consent, request, election, offer or acceptance is given or made pursuant to this Lease, it shall be in writing. Communications and payments shall be

addressed, if to the Landlord, at the Landlord's Address for Notices as set forth in Section 1.2 or at such other address as may have been specified by prior notice to the Tenant; and if to the Tenant, at the Tenant's Original Address or at such other place as may have been specified by prior notice to the Landlord. Any communication so addressed shall be deemed duly given on the earlier of (i) the date received, or (ii) on the next business day if sent by a nationally recognized overnight courier service. If the Landlord by notice to the Tenant at any time designates some other person to receive payments or notices, all payments or notices thereafter by the Tenant shall be paid or given to the agent designated until notice to the contrary is received by the Tenant from the Landlord. Notices to either party under this Lease may be given by legal counsel to such party.

Section 12.3 Successors and Limitation on Liability.

The obligations of this Lease shall run with the land, and this Lease shall be binding upon and inure to the benefit of the parties hereto and their respective successors and assigns, except that the original Landlord named herein and each successor Landlord shall be liable only for obligations accruing during the period of its ownership or otherwise reflected in a certificate delivered to it by Tenant pursuant to section 10.4 (or would have been reflected in such a certificate had one been timely requested). Neither the Tenant, nor anyone claiming by, under or through the Tenant, shall be entitled to obtain any judgment in enforcing the terms and conditions of this Lease creating personal liability on the part of the Landlord or enforcing any obligations of the Landlord against any assets of the Landlord other than its interest in the Property, and proceeds therefrom and, without limitation of the foregoing, in no event shall any personal liability arise on the part of any of the Landlord's officers, employees, directors or shareholders. Likewise, no personal liability shall arise on the part of the Tenant's officers, employees, directors or shareholders, as this Lease shall create liability on the part of the Tenant and not personal liability on the part of such officers, employees, directors or shareholders.

Section 12.4 Waivers.

The failure of the Landlord or the Tenant to seek redress for violation of, or to insist upon strict performance of, any covenant or condition of this Lease, shall not be deemed a waiver of such violation nor prevent a subsequent act, which would have originally constituted a violation, from having all the force and effect of an original violation. The receipt by the Landlord of Annual Fixed Rent or Additional Rent with knowledge of the breach of any covenant of this Lease shall not be deemed a waiver of such breach. No provision of this Lease shall be deemed to have been waived by the Landlord or the Tenant, as the case may be, unless such waiver be in writing signed by the Landlord or the Tenant, as the case may be. No consent or waiver, express or implied, by the Landlord or Tenant to or of any breach of any agreement or duty shall be construed as a waiver or consent to or of any other breach of the same or any other agreement or duty.

Section 12.5 Acceptance of Partial Payments of Rent.

No acceptance by either party of a lesser sum than the amount then due to such party shall be deemed to be other than a partial installment of such rent due, nor shall any endorsement or statement on any check or any letter accompanying any check or payment as rent be deemed

an accord and satisfaction, and either party may accept such check or payment without prejudice to the other party's right to recover the balance of such installment or pursue any other remedy in this Lease provided. The delivery of keys to any employee of the Landlord or to the Landlord's agent or any employee thereof shall not operate as a termination of this Lease or a surrender of the Premises.

Section 12.6 Interpretation and Partial Invalidity.

If any term of this Lease, or the application thereof to any person or circumstances, shall to any extent be invalid or unenforceable, the remainder of this Lease, or the application of such term to persons or circumstances other than those as to which it is invalid or unenforceable, shall not be affected thereby, and each term of this Lease shall be valid and enforceable to the fullest extent permitted by law. The titles of the Articles are for convenience only and not to be considered in construing this Lease. This Lease contains all of the agreements of the parties with respect to the subject matter thereof and supersedes all prior dealings between them with respect to such subject matter.

Section 12.7 Quiet Enjoyment.

So long as the Tenant pays Annual Fixed Rent and Additional Rent as and when due and no default on the part of Tenant exists beyond any applicable notice and cure period the Tenant shall peaceably and quietly have, hold and enjoy the Premises free of any claims by, through or under, or superior title to, the Landlord including, without limitation, any ground lessor, mortgagee, or manager of the Property.

Section 12.8 Brokerage.

Each party represents and warrants to the other that it has had no dealings with any broker or agent other than the Broker in connection with this Lease and shall indemnify and hold harmless the other from claims for any brokerage commission (other than by the Broker) arising out a breach of the foregoing representations. Landlord shall be responsible for any commission due to the Broker pursuant to the terms of a separate agreement.

Section 12.9 Surrender of Premises and Holding Over.

The Tenant shall surrender possession of the Premises on the last day of the Term and the Tenant waives the right to any notice of termination or notice to quit at the end of the Term. The Tenant covenants that upon the expiration or sooner termination of this Lease, it shall, without notice, deliver up and surrender possession of the Premises broom clean and in the same condition in which the Tenant has agreed to keep the same during the continuance of this Lease and in accordance with the terms hereof, normal wear and tear and damage by fire or other casualty excepted, first removing therefrom all personal property of the Tenant and any alterations or additions required to be removed pursuant to Section 4.2, and repairing all damage caused by such removal. Upon the expiration of this Lease or if the Premises should be abandoned by the Tenant, or this Lease should terminate for any cause, and at the time of such expiration, vacation, abandonment or termination, the Tenant or Tenant's agents, subtenants or any other person should leave any property of any kind or character on or in the Premises after

having vacated the Premises, the fact of such leaving of property on or in the Premises shall be conclusive evidence of intent by the Tenant, and individuals and entities deriving their rights through the Tenant, to abandon such property so left in or upon the Premises, and such leaving shall constitute abandonment of the property. Landlord shall have the right and authority without notice to the Tenant or anyone else, to remove and destroy, or to sell or authorize disposal of such property, or any part thereof, without being in any way liable to the Tenant therefor and the proceeds thereof shall belong to the Landlord as compensation for the removal and disposition of such property.

If the Tenant fails to surrender possession of the Premises upon the expiration or sooner termination of this Lease, then Tenant shall be deemed a tenant at sufferance only and Tenant shall pay to Landlord, as rent for any period after the expiration or sooner termination of this Lease an amount equal to one hundred fifty percent (150%) of the Annual Fixed Rent to be paid under this Lease, together with all Additional Rent required under this Lease. Acceptance by the Landlord of such payments shall not constitute a consent to a holdover hereunder or result in a renewal or extension of the Tenant's rights of occupancy. Such payments shall be in addition to and shall not affect or limit the Landlord's right of re entry, Landlord's right to collect such damages as may be available at law, or any other rights of the Landlord under this Lease or as provided by law.

Prior to the expiration of the Lease, Tenant shall clean and otherwise decommission all interior surfaces (including floors, walls, ceilings and counters), piping, supply lines, waste lines and plumbing in or serving the Premises, and all exhaust or other ductwork in or serving the Premises, in each case that has carried, released or otherwise been exposed to any Hazardous Material due to Tenant's use or occupancy of the Premises, and shall otherwise clean the Premises so as to permit the report hereinafter called for by this Section 11.10 to be issued. Prior to the expiration of this Lease (or within thirty (30) days after any earlier termination), Tenant, at Tenant's expense, shall obtain for Landlord a report addressed to Landlord (and, at Tenant's election, Tenant) by a reputable licensed environmental engineer or industrial hygienist that is designated by Tenant and acceptable to Landlord in Landlord's reasonable discretion, which report shall be based on the environmental engineer's or industrial hygienist's inspection of the Premises and shall state, to the Landlord's reasonable satisfaction, that (a) the Hazardous Materials described in the first sentence of this paragraph, to the extent if any, existing prior to such decommissioning, have been removed in accordance with applicable laws; (b) all Hazardous Materials described in the first sentence of this paragraph, if any, have been removed in accordance with applicable laws from the interior surfaces of the Premises (including floors, walls, ceilings, and counters), piping, supply lines, waste lines and plumbing, and all such exhaust or other ductwork in the Premises, may be re-used by a subsequent tenant or disposed of in compliance with applicable laws without incurring special costs or undertaking special procedures for demolition, disposal, investigation, assessment, cleaning or removal of such Hazardous Materials and without giving notice in connection with such Hazardous Materials; and (c) the Premises may be re-occupied for office or laboratory use, demolished or renovated without incurring special costs or undertaking special procedures for disposal, investigation, assessment, cleaning or removal of Hazardous Materials described in the first sentence of this paragraph and without giving notice in connection with Hazardous Materials. Further, for purposes of clauses (b) and (c), "special costs" or "special procedures" shall mean costs or procedures, as the case may be, that would not be incurred but for the nature of the Hazardous

Materials as Hazardous Materials instead of non-hazardous materials. The report shall also include reasonable detail concerning the clean-up measures taken, the clean-up locations, the tests run and the analytic results.

If Tenant fails to perform its obligations under this Section 11.10, without limiting any other right or remedy, Landlord may, on thirty (30) days' prior written notice to Tenant (except in an emergency when no prior notice shall be required) perform such obligations, at Tenant's expense, and Tenant shall, within thirty (30) days of demand, reimburse Landlord for all reasonable out-of-pocket costs and expenses incurred by Landlord in connection with such work. Tenant's obligations under this Section 11.10 shall survive the expiration or earlier termination of this Lease. In addition, at Landlord's election, Landlord may inspect the Premises and/or Property for Hazardous Materials at Landlord's cost and expenses, within thirty (30) days of Tenant's surrender of the Premises at the expiration or earlier termination of this Lease. Tenant shall pay for all such costs and expenses incurred by Landlord in connection with such inspection if such inspection reveals that a release or threat of release of Hazardous Materials exists at the Property or Premises as a result of the acts or omission of Tenant, its officers, employees, contractors, and agents (except to the extent resulting from the acts or omissions of Landlord or Landlord's agents, employees or contractors).

Section 12.10 Financial Reporting.

Tenant shall from time to time (but at least annually) on the anniversary of the Lease provide Landlord with financial statements of Tenant, together with related statements of Tenant's or its parent's operations for the most recent fiscal year then ended, certified to Landlord by an independent certified public accounting firm. Landlord agrees to keep such financial statements and related statements of operations confidential. If Tenant or its parent is a public company, in lieu of such certification, Landlord may refer to Tenant's or its parent's website for such information.

Section 12.11 No Consequential Damages.

In no event shall either Landlord or Tenant be liable to the other for consequential damages.

Section 12.12 Governing Law.

This Lease shall be governed by and construed in accordance with the laws of the Commonwealth of Massachusetts.

Section 12.13 Signage.

Landlord shall provide a listing identifying Tenant on the Building directory located in the Building lobby. Tenant shall be responsible for providing, at its sole cost and expense, signage at the entry to the Premises and any signage within the Premises. All signage pursuant to this Section 12.13 shall be consistent with Landlord's Signage and Design Standard, if any, applicable to the Building from time to time, and shall be subject to Landlord's approval, not to be unreasonably withheld, and the approval of applicable governmental authorities.

Section 12.14 Ground Lease.

This Lease is in all respects subject to the ground lease (the "Ground Lease") between the Landlord as lessee and Massachusetts Institute of Technology ("MIT") as lessor dated as of August 20, 1986. If any provision of the Ground Lease shall be inconsistent with the provisions of this Lease, the provisions of the Ground Lease shall be deemed to limit the provisions hereof, except as are expressly otherwise provided in a written agreement signed by MIT, the Landlord and the Tenant. Landlord represents and warrants to Tenant that the term of the Ground Lease extends for a period longer than the Term of this Lease, as the same may be extended pursuant to Section 2.6. This Lease is subject to the execution and delivery of a Non-Disturbance Agreement from MIT in the form attached hereto as Exhibit H.

Section 12.15 Cambridge Employment Plan.

The Tenant agrees to sign an agreement with the Employment and Training Agency designated by the City Manager of the City of Cambridge as provided in subsections (a) - (g) of Section 24-4 of Ordinance Number 1005 of the City of Cambridge, adopted April 23, 1984.

Section 12.16 Solvent Storage

Landlord shall manage the allocation of solvent storage quantities for tenants in the Building. Tenant shall be allocated its proportionate share of the allowable share of the Building's solvent storage capacity of 480 gallons (the fifth floor's allowable share is 44 gallons, the fourth floor's allowable share is 60 gallons), such storage to be located in the acid neutralization tank and chemical storage areas, as appropriate, as depicted on Exhibit C-1 (second page) attached hereto. All solvent storage by Tenant shall be subject to Tenant obtaining and maintaining all required governmental permitting.

Section 12.17 Protection of REIT Status.

In the event that Landlord determines that any of the financial obligations of Tenant to Landlord as set forth in this Lease might (a) fail to qualify as "rents from real property" within the meaning of Section 856(d) of the Internal Revenue Code of 1986, as amended (the "Code"), or (b) otherwise jeopardize the status of any of Landlord's affiliates, including Forest City Realty Trust, Inc., as a "real estate investment trust" ("REIT") within the meaning of Section 856 of the Code, then, at Landlord's option, Landlord may, in its sole discretion, assign any of its rights and obligations under this Lease to a designee chosen by Landlord for such purpose (which, in each case, shall be an affiliate of Landlord), or cause one or more such designees (which, in each case, shall be an affiliate of Landlord) to perform such activities to the extent required to maintain such status as a REIT, provided, however, that any assignment permitted pursuant to this Section shall not increase Tenant's obligations nor decrease Tenant's rights in this Lease, and shall not result in the imposition of any additional charge or expense upon Tenant.

IN WITNESS WHEREOF, this Lease has been executed and delivered as of the date first above written as a sealed instrument.

LANDLORD:

UP 26 LANDSDOWNE, LLC
a Delaware limited liability company

By: FC HCN University Park, LLC,
a Delaware limited liability company
Its Sole Member

By: Forest City University Park, LLC,
a Delaware limited liability company
Its Managing Member

By: /s/ Michael Farley
Name: Michael Farley
Title: Vice President

TENANT:

FULCRUM THERAPEUTICS, Inc.,
a Delaware corporation

By: /s/ Robert J. Gould
Name: Robert J. Gould
Title: President & C.E.O.

EXHIBIT A

BASIC LEASE TERMS

Building: 26 Landsdowne Street, Cambridge, MA

Premises: The Premises shall be comprised of approximately 28,731 rentable square feet as follows:
Floor 5: 21,736 rsf
Floor 4: 6,995 rsf

Annual Fixed Rent for the Term: \$76.00 per RSF as adjusted per the terms of Section 3.1 hereof.

Initial Term: Approximately ten (10) years and six (6) months, commencing at the Lease Commencement Date and expiring on the last day of the month in which the tenth (10th) anniversary of the Rent Commencement Date occurs, as set forth and in accordance with the terms of Section 2.5 hereof.

Extension Option: Tenant shall have one (1) option to extend the term of this Lease for an additional five (5) years, as described in Section 2.6 of the Lease.

Lease Commencement Date: As defined in Section 2.5 Anticipated to be the earlier of (i) December 1, 2017, or (ii) the date which is ten (10) days following notice from Landlord.

Landlord Delivery Date: The date determined in accordance with Section 2.5. Anticipated to be the earlier of (i) December 1, 2017, or (ii) the date which is ten (10) days following notice from Landlord.

Rent Commencement Date: The date determined in accordance with Section 2.5.

Leasehold Improvements Allowance: \$170.00 per rentable square foot or \$4,884,270.00

Total Rentable Area of Building: 102,876 rentable square feet

Security Deposit: \$1,091,778, to be provided pursuant to the terms of Article 11.

Parking Privileges: Commencing on the Rent Commencement Date and continuing through the Term, Tenant shall be entitled to use and shall pay for 1.5 parking passes per 1,000 rsf (which shall initially be equal to forty-three (43) parking passes) in accordance with Section 2.4 of the Lease. Subject to availability, Tenant shall have the right to lease additional parking spaces from Landlord; such lease for additional parking spaces shall be on a month-to-

month basis at the then-prevailing fair market value for such parking passes.

Permitted Uses:

Office and/or research and development, laboratory, and vivarium uses, and customary accessory uses supporting the foregoing.

Tenant's Address for Notices:

Before the Rent Commencement Date:

Fulcrum Therapeutics, Inc.
One Kendall Square
Building 700, B7102
Cambridge, Massachusetts 02139
Attention: Chief Executive Officer

After the Rent Commencement Date:

Fulcrum Therapeutics, Inc.
26 Landsdowne Street
Cambridge, Massachusetts 02139
Attention: Chief Executive Officer

With a copy to:

Wilmer Cutler Pickering Hale and Dorr LLP
60 State Street
Boston, Massachusetts 02109
Attention: Lia Der Marderosian, Esq.

Landlord's Original Address:

UP 26 Landsdowne, LLC
1100 Terminal Tower
50 Public Square
Cleveland, Ohio 44130
Attention: General Counsel

Landlord's Address for Notices:

UP 26 Landsdowne, LLC
c/o Forest City Commercial Group, LLC
38 Sidney Street, Suite 180
Cambridge, Massachusetts 02139-4234
Attention: Asset Manager



June 12, 2016

Robert J. Gould, Ph.D.
[**]

Re: Offer of Employment

Dear Robert:

Fulcrum Therapeutics, Inc. (the "Company") is pleased to confirm its offer to employ you as President and Chief Executive Officer. As President and Chief Executive Officer you will be a member of the Board and report to the Company's Board of Directors (the "Board"). Your start date will be no later than June 20, 2016 pending completion of all meetings with team members and signing of the new agreed upon Agreement with Epizyme.

Responsibilities are expected to include, but may not be limited to, the following:

- Oversee and integrate all company activities to ensure Fulcrum meets its research, development, and business milestones by focusing on value creation for our founders, employees, partners, investors and most importantly, making a difference in patients' lives
 - Work with the Board and senior management to develop and communicate a compelling vision, strategic direction and company business plan; continually evaluate alternative strategies; identify competitive issues; capitalize on the product engine and develop and implement operating plans to achieve objectives
 - Build a robust organization by ensuring that qualified research & development and business talent are recruited, hired and retained. Work with the Board and the senior management team to manage uncertainty while maintaining an entrepreneurial environment; manage performance of team by providing feedback, teaching and development opportunities
 - Foster an internal atmosphere that supports individual accountability, transparency, open communication and respect to enable employees to focus on the Company's culture and mission
 - Build and maintain a "Group Genius" environment for our founders, employees, advisors, key opinion leaders, partners and investors where everyone expresses their ideas and opinions and where we ultimately integrate these ideas to achieve the best plans and solutions for our patients
 - Develop, build and lead strategic partnerships with external companies to complement Fulcrum's capability, to raise dollars for building the company and to bring important products to the patients we serve
-

- Serve as the primary spokesperson for company, establishing and communicating the company's vision and image, and enhancing its visibility among potential partners

Your compensation for this position will be at the rate of \$420,000 a year, payable in accordance with the Company's normal pay schedule, which the Company currently expects will be bi-weekly. All payments are subject to legally required tax withholdings. It is expected that, when an annual bonus program is approved by the Board of Directors, you will be eligible for a target bonus at 35% of your annual compensation, based upon the achievement of corporate and individual goals, as agreed by the Board of Directors. You will be eligible to participate each year in any annual bonus plan adopted by the Company and the Company, subject to financial, business, and other circumstances and factors.

After Series A funding, you will be issued restricted stock grant for 3,000,000 shares of Fulcrum Therapeutics, Inc. common stock (the "Shares"), subject to approval of the Company's Board of Directors, at an exercise or purchase price equal to the fair market value of the Company's common stock on the date of grant or issuance, subject to the standard terms and conditions of Fulcrum Therapeutics, Inc. Stock Incentive Plan and form of stock option or restricted stock agreement, including vesting, subject to continued employment. The Shares shall vest over four years at the rate of 25% on the first anniversary of the commencement date of your employment and an additional 6.25% per quarter for the next twelve successive quarters of employment when, after four full years of employment, the Shares will be fully vested. The Share grant will be brought to the Board of Directors for approval soon after you begin employment with the Company.

The Company will offer a comprehensive benefits program and you will be eligible to participate in the program to the extent that the company establishes them soon after the completion of the Series A financing. You will accrue 15 paid vacation days each year for the first 5 years of service and receive all paid holidays annually in accordance with the company holiday schedule.

It is understood that you are an "at-will" employee. You are not being offered employment for a definite period of time, and either you or the Company may terminate the employment relationship at any time and for any reason, with or without Cause or prior notice and without additional compensation to you, other than as provided below.

(a) the Company may terminate your employment for "Cause" (as defined below) upon written notice to you effectively immediately, in which case you will not be entitled to receive any form of payment other than your earned compensation through your date of separation;

(b) you may terminate your employment voluntarily other than for “Good Reason” (as defined below) upon at least thirty (30) days’ prior written notice to the Company, in which case you will not be entitled to receive any form of payment other than your earned compensation through your date of separation; and

(c) Notwithstanding the foregoing, in the event that the Company terminates your employment without Cause, then, subject to you entering into and complying with a separation agreement and general release in a form provided by the Company, you will be entitled to a severance pay in an amount equal to: (i) twelve months of your then base salary as of the date of termination, such amount to be paid in equal installments over a twelve (12) month period after the date of your termination in accordance with the Company’s usual payroll practices and periods, subject to applicable taxes and withholding, (ii) payment for twelve (12) months of monthly COBRA premiums at the same rate as the Company pays for active employees for you and your eligible dependents, subject to applicable COBRA terms and in compliance with applicable non-discrimination or other requirements under the Internal Revenue Code (the “Code”), the Patient Protection and Affordable Care Act, or the Health Care and Education Reconciliation Act.

(d) For purposes of this letter agreement:

“Cause” means:

Your dishonest statements or acts with respect to the Company or any affiliate of the Company, or any current or prospective customers, suppliers vendors or other third parties with which such entity does business that results in or is reasonably anticipated to result in material harm to the Company; (ii) your conviction of (A) a felony or (B) any misdemeanor involving moral turpitude, deceit, dishonesty or fraud; (iii) your failure to perform your assigned duties and responsibilities to the reasonable satisfaction of the Company which failure continues, in the reasonable judgment of the Company, for thirty (30) days after written notice given to you by the Company describing such failure in reasonable detail; (iv) your gross negligence, willful misconduct or insubordination with respect to the Company that results in or is reasonably anticipated to result in material harm to the Company; or (v) your material violation of any provision of any agreement(s) between you and the Company relating to noncompetition, nonsolicitation, nondisclosure and/or assignment of inventions.

(e) For purposes of this letter, “Good Reason” means, in the context of your resignation from your employment position with the Company, a resignation that occurs within thirty (30) days following: (i) a change in the principal location at which you provide services to the Company beyond fifty (50) miles from Cambridge, MA; (ii) a material reduction in your compensation or a material reduction in your benefits, except such a reduction in connection with a general reduction in compensation or other benefits of all senior executives of the Company; (iii) a material breach of this letter by the Company that has not been cured within ten (10) days after written notice thereof by you to the Company; or (iv) a failure by the Company to obtain the assumption of this letter by any successor to the Company.

(f) The time for payment, or schedule for payment, of any severance payments due hereunder may not be accelerated, except as provided for in the Treasury Regulations promulgated under Section 409A of the Internal Revenue Code of 1986 (the “Code11), or any law replacing or superseding such Section or

regulations. Notwithstanding the preceding provisions of this Section 6(d), in the case that the Company becomes a publicly traded company and you are deemed a "specified employee" (as defined in Section 409A(2)(B)(i) of the Code), no severance payment may be made earlier than the date which is six (6) months after the termination of employment hereunder (or, if earlier, the date of the death of the Executive) if and to the extent required by applicable law or other rules of any stock exchange upon which any of shares of the Company's capital stock are then traded.

Enclosed is a "Non-Solicitation, Non-Competition, Confidentiality and Assignment Agreement" (the "Employee Agreement"). This offer of employment is conditioned on your willingness to enter into and abide by the terms of the Employee Agreement, the terms of which are incorporated into this offer letter.

In making this offer, the Company understands, and in accepting it you represent that you are not under any obligation to any former employer or any person or entity which would prevent, limit, or impair in any way the performance by you of your duties as an employee of the Company.

The Immigration Reform and Control Act requires employers to verify the employment eligibility and identity of new employees. You will be required to complete a Form I-9 which will be provided to you before the Start Date. Please bring the appropriate documents listed on that form with you when you report for work. We will not be able to employ you if you fail to comply with this requirement.

This offer letter and the Employee Agreement and Equity Documents referenced above constitute the complete agreement between you and the Company, contain all of the terms of your employment with the Company and supersede any prior agreements, representations or understandings (whether written, oral or implied) between you and the Company. Neither this offer letter nor the Employee Agreement may be amended or modified, except by an express written agreement signed by both you and a duly authorized officer of the Company, although, consistent with your at-will employment, your job duties, title, reporting relationship, compensation and benefits may change from time to time, at the Company's option.

Please indicate your acceptance of this offer by signing and returning the enclosed copy of this letter and the Employee Agreement no later than "-" based on when he is scheduled to come back to meet the rest of the team. You may indicate your acceptance of this offer by signing on the appropriate space below and returning a signed, scanned copy of this letter and the Employee Agreement to Chris Robinson, [**] and Susan O'Connor at [**].

We look forward to your joining the Company and are pleased that you will be working with us.

Very truly yours,

Mark Levin
Interim Chief Executive Officer
Fulcrum Therapeutics, Inc.

Accepted and Agreed:

/s/ Robert J. Gould
Robert J. Gould, Ph.D.

13 June 2016

Date



26 Landsdowne Street, 5th Floor
Cambridge, MA 02139
TEL (617) 651-8851
www.FulcrumTX.com

December 6, 2018

Bryan Stuart
[**]

Re: Offer of Employment

Dear Bryan,

Fulcrum Therapeutics, Inc. (the "Company") is pleased to confirm its offer to employ you as a Chief Operating Officer reporting to Robert Gould, President & CEO. As the COO you will be a key business partner with the CEO in building the company, setting and driving corporate strategy and long-range planning, and helping to lead and maintain strong relationships with the financial and business community. You will partner with the CEO and the leadership team to develop Fulcrum's long-term business strategy and assure continuous integration across Corporate Development, Scientific and Financial strategies. In this role, the COO is a key strategic partner focusing on future value creation for Fulcrum. This includes oversight for portfolio strategy including project planning and management, business development, operations, and patient advocacy.

Your effective date of hire as an employee will be a date agreed to by you and the Company. For purposes of this offer letter, the actual first day of your employment shall be referred to as the "Start Date". Your start date will be no later than December 17, 2018. Your normal place of work will be at the Company's offices in Cambridge, MA.

Your annual compensation for this position will be at the rate of \$400,000 per year, payable in accordance with the Company's normal pay schedule, which currently is semi-monthly ("Base Salary"). All payments are subject to legally required tax withholdings. In addition to your Base Salary, you will be eligible to earn an annual target bonus of up to 35% of your Base Salary. The actual amount of such bonus, if any, will be determined by the Company's Board of Directors (the "Board") and your manager in their good faith discretion, based upon achievement of corporate and individual goals. The bonus, if any, shall be paid at a time and in a manner as determined by the Company in its sole discretion. You must be employed by Fulcrum at the time of any such bonus payment to be eligible for any such payment. Because your start date is after October 1, 2018, you will not be eligible to participate in our 2018-year end compensation program (base salary/bonus/equity); you will be eligible to begin participating in 2019.



You will be issued a stock option grant for 2,125,000 shares of Fulcrum Therapeutics, Inc. stock (the "Options"), subject to approval of the Company's Board of Directors, at an exercise price equal to the fair market value of the Company's common stock on the date of grant or issuance, subject to the standard terms and conditions of Fulcrum Therapeutics, Inc. Stock Incentive Plan and form of stock option agreement, including vesting, subject to continued employment. Subject to the terms of the stock option agreement and your continued employment, the Options shall vest over four years at the rate of 25% on the first anniversary of the commencement date of your employment and an additional 6.25% per quarter for the next twelve successive quarters of employment when, after four full years of employment, the Options will be fully vested. The Options grant will be brought to the Board of Directors for approval soon after you begin employment with the Company.

You will be eligible to participate in the Company's health insurance programs as well as the life, AD&D, short and long-term disability plans, along with the Company's 401k plan, subject to the terms of those plans. As of January 1, 2019, Fulcrum now offers employees a discretionary vacation time off program. In addition, you will receive paid holidays in accordance with the annual company holiday schedule. Current Benefits Summary is attached. Benefits are subject to change at any time in the Company's sole discretion.

It is understood and agreed that that you are an "at-will" employee. You are not being offered employment for a definite period of time, and either you or the Company may terminate the employment relationship at any time and for any reason, with or without cause or prior notice and without additional compensation to you, other than as provided below:

Notwithstanding the foregoing, in the event that the Company terminates your employment without Cause (as defined below), and for the avoidance of doubt, not due to death or disability, then, subject to you entering into and complying with a separation agreement and general release in a form provided by the Company no later than sixty (60) days following termination of employment, you will be entitled to severance pay in an amount equal to:

- Six (6) months of your then current Base Salary, less lawful deductions, paid in equal installments in accordance with the Company's standard payroll practice over the six-month period immediately following your termination of employment (the "Severance Payments"); provided, that the first installment payment of the Severance Payments shall be made on the sixtieth (60th) day after the date of your termination, and will include payment of any installment payments that were otherwise due prior thereto; plus
 - subject to (i) your timely election of continuation coverage under COBRA, and (ii) your continued copayment of premiums at the same level and cost to you as if you were an employee of the Company (excluding, for purposes of calculating cost, an employee's ability to pay premiums with pre-tax dollars), continued payment by the
-

Company of your (and your dependents, if applicable) health, insurance coverage during the six (6) month period following the date of termination to the same extent that the Company paid for such coverage immediately prior to the date of termination, in a manner intended to avoid any excise tax under Section 4980D of the Internal Revenue Code of 1986, as amended, subject to the eligibility requirements and other terms and conditions of such insurance coverage.

For purposes of this letter agreement:

“Cause” means:

(i) Your dishonest statements or acts with respect to the Company or any affiliate of the Company, or any current or prospective customers, suppliers vendors or other third parties with which such entity does business that results in or is reasonably anticipated to result in material harm to the Company; (ii) your conviction of (A) a felony or (B) any misdemeanor involving moral turpitude, deceit, dishonesty or fraud; (iii) your gross negligence, willful misconduct or insubordination with respect to the Company that results in or is reasonably anticipated to result in material harm to the Company; or (iv) your material violation of any provision of any agreement(s) between you and the Company relating to nonsolicitation, nondisclosure and/or assignment of inventions.

Section 409A.

Although the Company does not guarantee the tax treatment of any payments under this letter agreement, the intent of the Company is that the payments and benefits under this letter agreement be exempt from, or comply with, Section 409A of the Internal Revenue Code of 1986, as amended, and all Treasury Regulations and guidance promulgated thereunder (“Code Section 409A”) and to the maximum extent permitted the Agreement shall be limited, construed and interpreted in accordance with such intent. In no event whatsoever shall the Company or its affiliates or their respective officers, directors, employees or agents be liable for any additional tax, interest or penalties that may be imposed on you by Code Section 409A or damages for failing to comply with Code Section 409A.

Notwithstanding any other provision of this letter agreement to the contrary, to the extent that any reimbursement of expenses constitutes “deferred compensation” under Code Section 409A, such reimbursement shall be provided no later than December 31 of the year following the year in which the expense was incurred. The amount of expenses reimbursed in one year shall not affect the amount eligible for reimbursement in any subsequent year. The amount of any in-kind benefits provided in one year shall not affect the amount of in-kind benefits provided in any other year.

For purposes of Code Section 409A (including, without limitation, for purposes of Treasury Regulation Section 1.409A-2(b)(2)(iii)), the right to receive payments in the form of installment payments shall be treated as a right to receive a series of separate payments and, accordingly, each installment payment shall at all times be considered a separate and distinct payment.

Notwithstanding any other provision of this letter agreement to the contrary, if at the time of your separation from service (as defined in Code Section 409A), you are a "Specified Employee", then the Company will defer the payment or commencement of any nonqualified deferred compensation subject to Code Section 409A payable upon separation from service (without any reduction in such payments or benefits ultimately paid or provided to you) until the date that is six (6) months following separation from service or, if earlier, the earliest other date as is permitted under Code Section 409A (and any amounts that otherwise would have been paid during this deferral period will be paid in a lump sum on the day after the expiration of the six (6) month period or such shorter period, if applicable).

This offer of employment is contingent upon you're signing the Employee Confidentiality and Assignment Agreement (the "Employee Agreement") and receipt of a satisfactory outcome of pre-employment screening activities including favorable reference checks of former employment, verification of your ability to work in the United States, education and criminal history check. In making this offer, the Company understands, and in accepting it you represent that you are not under any obligation to any former employer or any person or entity which would prevent, limit, or impair in any way the performance by you of your duties as an employee of the Company.

The Immigration Reform and Control Act requires employers to verify the employment eligibility and identity of new employees. You will be required to complete a Form I-9 which will be provided to you before the Start Date. Please bring the appropriate documents listed on that form with you when you report for work. We will not be able to employ you if you fail to comply with this requirement.

This offer letter and the Employee Agreement and Equity Documents referenced above constitute the complete agreement between you and the Company, contain all the terms of your employment with the Company and supersede any prior agreements, representations or understandings (whether written, oral or implied) between you and the Company. Neither this offer letter nor the Employee Agreement may be amended or modified, except by an express written agreement signed by both you and a duly authorized officer of the Company, although, consistent with your at-will employment, your job duties, title, reporting relationship, compensation and benefits may change from time to time, at the Company's option.

Please indicate your acceptance of this offer by signing and returning the enclosed copy of this letter and the Employee Agreement. You may indicate your acceptance of this offer by signing on the appropriate space below and returning a signed, scanned copy of this letter to Kim Hazen at [**].

We look forward to your joining Fulcrum and are pleased that you will be working with us.

Very truly yours,

/s/ Robert Gould

Robert Gould, Ph.D.
President & CEO

Accepted and Agreed:

/s/ Bryan Stuart
Bryan Stuart

12/6/18
Date

August 9, 2016

Diego Cadavid, M.D.

[**]

Re: Offer of Employment

Dear Diego,

Fulcrum Therapeutics, Inc. (the “Company”) is pleased to confirm its offer to employ you as Vice President, Clinical Development. As Vice President, clinical development, you will report into Robert Gould, PhD, President and Chief Executive Officer. Your effective date of hire as a regular, full-time employee (the “Start Date”) will be September 6, 2016. Your normal place of work will be at the Company’s offices in Cambridge, MA.

Your compensation for this position will be at the rate of \$330,000 a year, payable in accordance with the Company’s normal pay schedule, which the Company currently expects will be bi-weekly. All payments are subject to legally required tax withholdings. It is expected that, when an annual bonus program is approved by the Board of Directors, you will be eligible for a target bonus at 25% of your annual compensation, based upon the achievement of corporate and individual goals, as agreed by the Board of Directors. You will be eligible to participate each year in any annual bonus plan adopted by the Company and the Company, subject to financial business, and other circumstances and factors.

In addition, the Company will provide you with a one-time sign-on bonus of \$150,000 which will be paid to you in two installments. You will receive the first payment of \$125,000 during your first month of employment and it will be subject to customary deductions and withholdings as required by law. You will receive the second payment of \$25,000 upon the first anniversary of your Start Date with the Company. Should you voluntarily leave the Company, other than for death or disability, within 12 months of receiving either payment, you will be obligated to return the gross amount of the payment to the company within 30 Days of your departure date.

After Series A funding, you will be issued either a stock option or restricted stock grant for 400,000 shares of Fulcrum Therapeutics, Inc. common stock (the “Shares”), subject to approval of the Company’s Board of Directors, at an exercise or purchase price equal to the fair market value of the Company’s common stock on the date of grant or issuance, subject to the standard terms and conditions of Fulcrum Therapeutics, Inc. Stock Incentive Plan and form of stock option or restricted stock agreement, including vesting, subject to continued employment. The Shares shall vest over four years at the rate of 25% on the first anniversary of the commencement date of your employment and an additional 6.25% per quarter for the next twelve successive quarters of employment when, after four full years of employment, the Shares will be fully vested. The Share grant will be brought to the Board of Directors for approval soon after you begin employment with the Company.

The Company will offer a comprehensive benefits program and you will be eligible to participate in the program to the extent that the company establishes them soon after the completion of the Series A financing. You will accrue 15 paid vacation days each year for the first 5 years of service and receive 12 paid holidays annually in accordance with the company holiday schedule.

It is understood and agreed that that you are an “at-will” employee. You are not being offered employment for a definite period of time, and either you or the Company may terminate the employment relationship at any time and for any reason, with or without cause or prior notice and without additional compensation to you except for your salary through the last day of your employment plus any then accrued but unused vacation.

Enclosed is a “Non-Solicitation, Non-Competition, Confidentiality and Assignment Agreement” (the “Employee Agreement”). This offer of employment is conditioned on your willingness to enter into and abide by the terms of the Employee Agreement, the terms of which are incorporated into this offer letter.

In making this offer, the Company understands, and in accepting it you represent that you are not under any obligation to any former employer or any person or entity which would prevent, limit, or impair in any way the performance by you of your duties as an employee of the Company.

The Immigration Reform and Control Act requires employers to verify the employment eligibility and identity of new employees. You will be required to complete a Form I-9 which will be provided to you before the Start Date. Please bring the appropriate documents listed on that form with you when you report for work. We will not be able to employ you if you fail to comply with this requirement.

This offer letter and the Employee Agreement and Equity Documents referenced above constitute the complete agreement between you and the Company, contain all of the terms of your employment with the Company and supersede any prior agreements, representations or understandings (whether written, oral or implied) between you and the Company. Neither this offer letter nor the Employee Agreement may be amended or modified, except by an express written agreement signed by both you and a duly authorized officer of the Company, although, consistent with your at-will employment, your job duties, title, reporting relationship, compensation and benefits may change from time to time, at the Company’s option.

Please indicate your acceptance of this offer by signing and returning the enclosed copy of this letter and the Employee Agreement no later than August 10, 2016. You may indicate your acceptance of this offer by signing on the appropriate space below and returning a signed, scanned copy of this letter and the Employee Agreement to Susan O’Connor at [**]

We look forward to your joining the Company and are pleased that you will be working with us.

Very truly yours,

/s/ Robert Gould

Robert Gould
President and Chief Executive Officer
Fulcrum Therapeutics, Inc.

Accepted and Agreed:

/s/ Diego Cadavid

Diego Cadavid, M.D.

Date 10 August 2016

INDEMNIFICATION AGREEMENT

This Indemnification Agreement (“Agreement”) is made as of [], 20[] by and between Fulcrum Therapeutics, Inc., a Delaware corporation (the “Company”), and [] (“Indemnitee”) [*Solely with respect to officers and directors that execute this form of indemnification agreement on or prior to the Company’s initial public offering:*] and shall be effective as of the effectiveness of a Registration Statement on Form S-1 relating to the initial registration under the Securities Act of 1933, as amended, of shares of the Company’s common stock].

RECITALS

WHEREAS, highly competent persons have become more reluctant to serve publicly-held corporations as directors or officers or in other capacities unless they are provided with adequate protection through insurance or adequate indemnification against inordinate risks of claims and actions against them arising out of their service to and activities on behalf of the corporation;

WHEREAS, the Board of Directors of the Company (the “Board”) has determined that, in order to attract and retain qualified individuals, the Company will attempt to maintain on an ongoing basis, at its sole expense, liability insurance to protect persons serving the Company and its subsidiaries from certain liabilities. Although the furnishing of such insurance has been a customary and widespread practice among United States-based corporations and other business enterprises, the Company believes that, given current market conditions and trends, such insurance may be available to it in the future only at higher premiums and with more exclusions. At the same time, directors, officers, and other persons in service to corporations or business enterprises are being increasingly subjected to expensive and time-consuming litigation relating to, among other things, matters that traditionally would have been brought only against the Company or business enterprise itself. The Certificate of Incorporation of the Company (as the same may be amended from time to time, the “Certificate of Incorporation”) requires indemnification of the officers and directors of the Company. Indemnitee may also be entitled to indemnification pursuant to the General Corporation Law of the State of Delaware (the “DGCL”). The Certificate of Incorporation and the DGCL expressly provide that the indemnification provisions set forth therein are not exclusive, and thereby contemplate that contracts may be entered into between the Company and members of the Board, officers and other persons with respect to indemnification;

WHEREAS, the uncertainties relating to such insurance and to indemnification have increased the difficulty of attracting and retaining such persons;

WHEREAS, the Board has determined that the increased difficulty in attracting and retaining such persons is detrimental to the best interests of the Company and its stockholders and that the Company should act to assure such persons that there will be increased certainty of such protection in the future;

WHEREAS, it is reasonable, prudent and necessary for the Company contractually to obligate itself to indemnify, and to advance expenses on behalf of, such persons to the fullest extent permitted by applicable law so that they will serve or continue to serve the Company free from undue concern that they will not be so indemnified;

WHEREAS, this Agreement is a supplement to and in furtherance of the Certificate of

Incorporation and any resolutions adopted pursuant thereto, and shall not be deemed a substitute therefor, nor to diminish or abrogate any rights of Indemnitee thereunder; and

[WHEREAS, Indemnitee is a representative of [·] [and its affiliated investment funds] (the “Fund”), and has certain rights to indemnification and/or insurance provided by the Fund which Indemnitee and the Fund intend to be secondary to the primary obligation of the Company to indemnify Indemnitee as provided herein, with the Company’s acknowledgement and agreement to the foregoing being a material condition to Indemnitee’s willingness to serve on the Board;]

WHEREAS, Indemnitee does not regard the protection available under the Certificate of Incorporation and insurance as adequate in the present circumstances, and may not be willing to serve as an officer or director without adequate protection, and the Company desires Indemnitee to serve in such capacity. Indemnitee is willing to serve, continue to serve and to take on additional service for or on behalf of the Company on the condition that he be so indemnified.

NOW, THEREFORE, in consideration of the premises and the covenants contained herein, the Company and Indemnitee do hereby covenant and agree as follows:

Section 1. Services to the Company. Indemnitee agrees to serve as [a][an] [officer][director] of the Company. Indemnitee may at any time and for any reason resign from such position (subject to any other contractual obligation or any obligation imposed by operation of law), in which event the Company shall have no obligation under this Agreement to continue Indemnitee in such position. This Agreement shall not be deemed an employment contract between the Company (or any of its subsidiaries or any Enterprise) and Indemnitee. Indemnitee specifically acknowledges that Indemnitee’s employment with the Company (or any of its subsidiaries or any Enterprise), if any, is at will, and the Indemnitee may be discharged at any time for any reason, with or without cause, except as may be otherwise provided in any written employment contract between Indemnitee and the Company (or any of its subsidiaries or any Enterprise), other applicable formal severance policies duly adopted by the Board, or, with respect to service as a director or officer of the Company, by the Certificate of Incorporation, the Company’s Bylaws, and the DGCL. The foregoing notwithstanding, this Agreement shall continue in force after Indemnitee has ceased to serve as [a][an] [officer][director] of the Company, as provided in Section 16 hereof.

Section 2. Definitions. As used in this Agreement:

(a) References to “agent” shall mean any person who is or was a director, officer, or employee of the Company or a subsidiary of the Company or other person authorized by the Company to act for the Company, to include such person serving in such capacity as a director, officer, employee, fiduciary or other official of another corporation, partnership, limited liability company, joint venture, trust or other enterprise at the request of, for the convenience of, or to represent the interests of the Company or a subsidiary of the Company.

(b) A “Change in Control” shall be deemed to occur upon the earliest to occur after the date of this Agreement of any of the following events:

i. Acquisition of Stock by Third Party. Any Person (as defined below) is or becomes the Beneficial Owner (as defined below), directly or indirectly, of securities of the

Company representing fifty percent (50%) or more of the combined voting power of the Company's then outstanding securities unless the change in relative Beneficial Ownership of the Company's securities by any Person results solely from a reduction in the aggregate number of outstanding shares of securities entitled to vote generally in the election of directors;

ii. Change in Board of Directors. During any period of two (2) consecutive years (not including any period prior to the execution of this Agreement), individuals who at the beginning of such period constitute the Board, and any new director (other than a director designated by a person who has entered into an agreement with the Company to effect a transaction described in Sections 2(b)(i), 2(b)(iii) or 2(b)(iv)) whose election by the Board or nomination for election by the Company's stockholders was approved by a vote of at least two-thirds of the directors then still in office who either were directors at the beginning of the period or whose election or nomination for election was previously so approved, cease for any reason to constitute at least a majority of the members of the Board;

iii. Corporate Transactions. The effective date of a merger or consolidation of the Company with any other entity, other than a merger or consolidation which would result in the voting securities of the Company outstanding immediately prior to such merger or consolidation continuing to represent (either by remaining outstanding or by being converted into voting securities of the surviving entity or its ultimate parent, as applicable) more than fifty-one percent (51%) of the combined voting power of the voting securities of the surviving entity or its ultimate parent, as applicable, outstanding immediately after such merger or consolidation and with the power to elect at least a majority of the board of directors or other governing body of such surviving entity or its ultimate parent, as applicable;

iv. Liquidation or Sale of Assets. The approval by the stockholders of the Company of a complete liquidation of the Company or an agreement for the sale or disposition by the Company of all or substantially all of the Company's assets; and

v. Other Events. There occurs any other event of a nature that would be required to be reported in response to Item 6(e) of Schedule 14A of Regulation 14A (or a response to any similar item on any similar schedule or form) promulgated under the Exchange Act (as defined below), whether or not the Company is then subject to such reporting requirement.

For purposes of this Section 2(b), the following terms shall have the following meanings:

(A) "Exchange Act" shall mean the Securities Exchange Act of 1934, as amended from time to time.

(B) "Person" shall have the meaning as set forth in Sections 13(d) and 14(d) of the Exchange Act; provided, however, that Person shall exclude (i) the Company, (ii) any trustee or other fiduciary holding securities under an employee benefit plan of the Company, and (iii) any corporation owned, directly or indirectly, by the stockholders of the Company in substantially the same proportions as their ownership of stock of the Company.

(C) "Beneficial Owner" shall have the meaning given to such term in Rule 13d-3 under the Exchange Act; provided, however, that Beneficial Owner

shall exclude any Person otherwise becoming a Beneficial Owner by reason of the stockholders of the Company approving a merger of the Company with another entity.

(c) "Corporate Status" describes the status of a person who is or was a director, officer, employee or agent of the Company or of any other corporation, limited liability company, partnership or joint venture, trust or other enterprise which such person is or was serving at the request of the Company.

(d) "Disinterested Director" shall mean a director of the Company who is not and was not a party to the Proceeding in respect of which indemnification is sought by Indemnitee.

(e) "Enterprise" shall mean the Company and any other corporation, limited liability company, partnership, joint venture, trust or other enterprise of which Indemnitee is or was serving at the request of the Company as a director, officer, trustee, partner, managing member, employee, agent or fiduciary.

(f) "Expenses" shall include all reasonable attorneys' fees, retainers, court costs, transcript costs, fees of experts and other professionals, witness fees, travel expenses, duplicating costs, printing and binding costs, telephone charges, postage, delivery service fees, any federal, state, local or foreign taxes imposed on Indemnitee as a result of the actual or deemed receipt of any payments under this Agreement, ERISA excise taxes and penalties, and all other disbursements or expenses of the types customarily incurred in connection with prosecuting, defending, preparing to prosecute or defend, investigating, being or preparing to be a witness in, or otherwise participating in, a Proceeding. Expenses also shall include (i) Expenses incurred in connection with any appeal resulting from any Proceeding, including without limitation the premium, security for, and other costs relating to any cost bond, supersedeas bond, or other appeal bond or its equivalent, and (ii) for purposes of Section 14(d) only, Expenses incurred by Indemnitee in connection with the interpretation, enforcement or defense of Indemnitee's rights under this Agreement, by litigation or otherwise. The parties agree that for the purposes of any advancement of Expenses for which Indemnitee has made written demand to the Company in accordance with this Agreement, all Expenses included in such demand that are certified by affidavit of Indemnitee's counsel as being reasonable shall be presumed conclusively to be reasonable. Expenses, however, shall not include amounts paid in settlement by Indemnitee or the amount of judgments or fines against Indemnitee.

(g) "Independent Counsel" shall mean a law firm, or a member of a law firm, that is experienced in matters of corporation law and neither presently is, nor in the past five years has been, retained to represent: (i) the Company or Indemnitee in any matter material to either such party (other than with respect to matters concerning the Indemnitee under this Agreement, or of other indemnitees under similar indemnification agreements), or (ii) any other party to the Proceeding giving rise to a claim for indemnification hereunder. Notwithstanding the foregoing, the term "Independent Counsel" shall not include any person who, under the applicable standards of professional conduct then prevailing, would have a conflict of interest in representing either the Company or Indemnitee in an action to determine Indemnitee's rights under this Agreement. The Company agrees to pay the reasonable fees and expenses of the Independent Counsel referred to above and to fully indemnify such counsel against any and all Expenses, claims, liabilities and damages arising out of or relating to this Agreement or its engagement pursuant hereto.

(h) The term “Proceeding” shall include any threatened, pending or completed action, suit, claim, counterclaim, cross claim, arbitration, mediation, alternate dispute resolution mechanism, investigation, inquiry, administrative hearing or any other actual, threatened or completed proceeding, whether brought in the right of the Company or otherwise and whether of a civil, criminal, administrative, legislative, or investigative (formal or informal) nature, including any appeal therefrom, in which Indemnitee was, is or will be involved as a party, potential party, non-party witness or otherwise by reason of the fact that Indemnitee is or was a director or officer of the Company, by reason of any action taken by him (or a failure to take action by him) or of any action (or failure to act) on his part while acting pursuant to his Corporate Status, in each case whether or not serving in such capacity at the time any liability or Expense is incurred for which indemnification, reimbursement, or advancement of Expenses can be provided under this Agreement. If the Indemnitee believes in good faith that a given situation may lead to or culminate in the institution of a Proceeding, this shall be considered a Proceeding under this paragraph.

(i) Reference to “other enterprise” shall include employee benefit plans; references to “fines” shall include any excise tax assessed with respect to any employee benefit plan; references to “serving at the request of the Company” shall include any service as a director, officer, employee or agent of the Company which imposes duties on, or involves services by, such director, officer, employee or agent with respect to an employee benefit plan, its participants or beneficiaries; and a person who acted in good faith and in a manner he reasonably believed to be in the best interests of the participants and beneficiaries of an employee benefit plan shall be deemed to have acted in manner “not opposed to the best interests of the Company” as referred to in this Agreement.

Section 3. Indemnity in Third-Party Proceedings. The Company shall indemnify Indemnitee in accordance with the provisions of this Section 3 if Indemnitee is, or is threatened to be made, a party to or a participant in any Proceeding, other than a Proceeding by or in the right of the Company to procure a judgment in its favor. Pursuant to this Section 3, Indemnitee shall be indemnified to the fullest extent permitted by applicable law against all Expenses, judgments, fines and amounts paid in settlement (including all interest, assessments and other charges paid or payable in connection with or in respect of such Expenses, judgments, fines and amounts paid in settlement) actually and reasonably incurred by Indemnitee or on his behalf in connection with such Proceeding or any claim, issue or matter therein, if Indemnitee acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the Company and, in the case of a criminal Proceeding had no reasonable cause to believe that his conduct was unlawful. The parties hereto intend that this Agreement shall provide to the fullest extent permitted by law for indemnification in excess of that expressly permitted by statute, including, without limitation, any indemnification provided by the Certificate of Incorporation, the Bylaws, vote of its stockholders or disinterested directors or applicable law.

Section 4. Indemnity in Proceedings by or in the Right of the Company. The Company shall indemnify Indemnitee in accordance with the provisions of this Section 4 if Indemnitee is, or is threatened to be made, a party to or a participant in any Proceeding by or in the right of the Company to procure a judgment in its favor. Pursuant to this Section 4, Indemnitee shall be indemnified to the fullest extent permitted by applicable law against all Expenses actually and reasonably incurred by him or on his behalf in connection with such Proceeding or any claim, issue or matter therein, if Indemnitee acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the Company. No indemnification for Expenses shall be

made under this Section 4 in respect of any claim, issue or matter as to which Indemnitee shall have been finally adjudged by a court to be liable to the Company, unless and only to the extent that the Chancery Court of the State of Delaware (the "Delaware Court") or any court in which the Proceeding was brought shall determine upon application that, despite the adjudication of liability but in view of all the circumstances of the case, Indemnitee is fairly and reasonably entitled to indemnification for such Expenses as the Delaware Court or other court shall deem proper.

Section 5. Indemnification for Expenses of a Party Who is Wholly or Partly Successful. Notwithstanding any other provisions of this Agreement, to the fullest extent permitted by applicable law and to the extent that Indemnitee is a party to (or a participant in) and is successful, on the merits or otherwise, in any Proceeding or in defense of any claim, issue or matter therein, in whole or in part, the Company shall indemnify Indemnitee against all Expenses actually and reasonably incurred by him in connection therewith. If Indemnitee is not wholly successful in such Proceeding but is successful, on the merits or otherwise, as to one or more but less than all claims, issues or matters in such Proceeding, the Company shall indemnify Indemnitee against all Expenses actually and reasonably incurred by him or on his behalf in connection with or related to each successfully resolved claim, issue or matter to the fullest extent permitted by law. For purposes of this Section and without limitation, the termination of any claim, issue or matter in such a Proceeding by dismissal, with or without prejudice, shall be deemed to be a successful result as to such claim, issue or matter.

Section 6. Indemnification For Expenses of a Witness. Notwithstanding any other provision of this Agreement, to the fullest extent permitted by applicable law and to the extent that Indemnitee is, by reason of his Corporate Status, a witness or otherwise asked to participate in any Proceeding to which Indemnitee is not a party, he shall be indemnified against all Expenses actually and reasonably incurred by him or on his behalf in connection therewith.

Section 7. Partial Indemnification. If Indemnitee is entitled under any provision of this Agreement to indemnification by the Company for some or a portion of Expenses, but not, however, for the total amount thereof, the Company shall nevertheless indemnify Indemnitee for the portion thereof to which Indemnitee is entitled.

Section 8. Additional Indemnification.

(a) Notwithstanding any limitation in Sections 3, 4, or 5, the Company shall indemnify Indemnitee to the fullest extent permitted by applicable law if Indemnitee is a party to or threatened to be made a party to any Proceeding (including a Proceeding by or in the right of the Company to procure a judgment in its favor) against all Expenses, judgments, fines and amounts paid in settlement (including all interest, assessments and other charges paid or payable in connection with or in respect of such Expenses, judgments, fines and amounts paid in settlement) actually and reasonably incurred by Indemnitee in connection with the Proceeding.

(b) For purposes of Section 8(a), the meaning of the phrase "to the fullest extent permitted by applicable law" shall include, but not be limited to:

i. to the fullest extent permitted by the provision of the DGCL that authorizes or contemplates additional indemnification by agreement, or the corresponding provision of any amendment to or replacement of the DGCL, and

ii. to the fullest extent authorized or permitted by any amendments to or replacements of the DGCL adopted after the date of this Agreement that increase the extent to which a corporation may indemnify its officers and directors.

Section 9. Exclusions. Notwithstanding any provision in this Agreement, the Company shall not be obligated under this Agreement to make any indemnification payment in connection with any claim made against Indemnitee:

(a) for which payment has actually been made to or on behalf of Indemnitee under any insurance policy or other indemnity provision, except with respect to any excess beyond the amount paid under any insurance policy or other indemnity provision; or

(b) for (i) an accounting of profits made from the purchase and sale (or sale and purchase) by Indemnitee of securities of the Company within the meaning of Section 16(b) of the Exchange Act (as defined in Section 2(b) hereof) or similar provisions of state statutory law or common law, or (ii) any reimbursement of the Company by the Indemnitee of any bonus or other incentive-based or equity-based compensation or of any profits realized by the Indemnitee from the sale of securities of the Company, as required in each case under the Exchange Act (including any such reimbursements that arise from an accounting restatement of the Company pursuant to Section 304 of the Sarbanes-Oxley Act of 2002 (the "Sarbanes-Oxley Act"), or the payment to the Company of profits arising from the purchase and sale by Indemnitee of securities in violation of Section 306 of the Sarbanes-Oxley Act); or

(c) except as provided in Section 14(d) of this Agreement, in connection with any Proceeding (or any part of any Proceeding) initiated by Indemnitee, including any Proceeding (or any part of any Proceeding) initiated by Indemnitee against the Company or its directors, officers, employees or other indemnitees, unless (i) the Board authorized the Proceeding (or any part of any Proceeding) prior to its initiation or (ii) the Company provides the indemnification, in its sole discretion, pursuant to the powers vested in the Company under applicable law.

Section 10. Advances of Expenses. Notwithstanding any provision of this Agreement to the contrary (other than Section 14(d)), the Company shall advance, to the extent not prohibited by law, the Expenses incurred by Indemnitee in connection with any Proceeding (or any part of any Proceeding) not initiated by Indemnitee, and such advancement shall be made within thirty (30) days after the receipt by the Company of a statement or statements requesting such advances from time to time, whether prior to or after final disposition of any Proceeding. Advances shall be unsecured and interest free. Advances shall be made without regard to Indemnitee's ability to repay the Expenses and without regard to Indemnitee's ultimate entitlement to indemnification under the other provisions of this Agreement. In accordance with Section 14(d), advances shall include any and all reasonable Expenses incurred pursuing an action to enforce this right of advancement, including Expenses incurred preparing and forwarding statements to the Company to support the advances claimed. The Indemnitee shall qualify for advances upon the execution and delivery to the Company of this Agreement, which shall constitute an undertaking providing that the Indemnitee undertakes to repay the amounts advanced (without interest) to the extent that it is ultimately determined that Indemnitee is not entitled to be indemnified by the Company. No other form of undertaking shall be required other than the execution of this Agreement. This Section 10 shall not apply to any claim made by Indemnitee for which indemnity is excluded pursuant to Section 9.

Section 11. Procedure for Notification and Defense of Claim.

(a) Indemnitee shall notify the Company in writing of any matter with respect to which Indemnitee intends to seek indemnification or advancement of Expenses hereunder as soon as reasonably practicable following the receipt by Indemnitee of written notice thereof. The written notification to the Company shall include a description of the nature of the Proceeding and the facts underlying the Proceeding. To obtain indemnification under this Agreement, Indemnitee shall submit to the Company a written request, including therein or therewith such documentation and information as is reasonably available to Indemnitee and is reasonably necessary to determine whether and to what extent Indemnitee is entitled to indemnification following the final disposition of such Proceeding. The omission by Indemnitee to notify the Company hereunder will not relieve the Company from any liability which it may have to Indemnitee hereunder or otherwise than under this Agreement, and any delay in so notifying the Company shall not constitute a waiver by Indemnitee of any rights under this Agreement. The Secretary of the Company shall, promptly upon receipt of such a request for indemnification, advise the Board in writing that Indemnitee has requested indemnification.

(b) The Company will be entitled to participate in the Proceeding at its own expense.

Section 12. Procedure Upon Application for Indemnification.

(a) Upon written request by Indemnitee for indemnification pursuant to Section 11(a), a determination, if required by applicable law, with respect to Indemnitee's entitlement thereto shall be made in the specific case: (i) if a Change in Control shall have occurred, by Independent Counsel in a written opinion to the Board, a copy of which shall be delivered to Indemnitee; or (ii) if a Change in Control shall not have occurred, (A) by a majority vote of the Disinterested Directors, even though less than a quorum of the Board, (B) by a committee of Disinterested Directors designated by a majority vote of the Disinterested Directors, even though less than a quorum of the Board, (C) if there are no such Disinterested Directors or, if such Disinterested Directors so direct, by Independent Counsel in a written opinion to the Board, a copy of which shall be delivered to Indemnitee or (D) if so directed by the Board, by the stockholders of the Company; and, if it is so determined that Indemnitee is entitled to indemnification, payment to Indemnitee shall be made within ten (10) days after such determination. Indemnitee shall cooperate with the person, persons or entity making such determination with respect to Indemnitee's entitlement to indemnification, including providing to such person, persons or entity upon reasonable advance request any documentation or information which is not privileged or otherwise protected from disclosure and which is reasonably available to Indemnitee and reasonably necessary to such determination. Any costs or Expenses (including attorneys' fees and disbursements) incurred by Indemnitee in so cooperating with the person, persons or entity making such determination shall be borne by the Company (irrespective of the determination as to Indemnitee's entitlement to indemnification) and the Company hereby indemnifies and agrees to hold Indemnitee harmless therefrom. The Company promptly will advise Indemnitee in writing with respect to any determination that Indemnitee is or is not entitled to indemnification, including a description of any reason or basis for which indemnification has been denied.

(b) In the event the determination of entitlement to indemnification is to be made by Independent Counsel pursuant to Section 12(a) hereof, the Independent Counsel shall be

selected as provided in this Section 12(b). If a Change in Control shall not have occurred, the Independent Counsel shall be selected by the Board, and the Company shall give written notice to Indemnitee advising him of the identity of the Independent Counsel so selected. If a Change in Control shall have occurred, the Independent Counsel shall be selected by Indemnitee (unless Indemnitee shall request that such selection be made by the Board, in which event the preceding sentence shall apply), and Indemnitee shall give written notice to the Company advising it of the identity of the Independent Counsel so selected. In either event, Indemnitee or the Company, as the case may be, may, within ten (10) days after such written notice of selection shall have been given, deliver to the Company or to Indemnitee, as the case may be, a written objection to such selection; provided, however, that such objection may be asserted only on the ground that the Independent Counsel so selected does not meet the requirements of "Independent Counsel" as defined in Section 2 of this Agreement, and the objection shall set forth with particularity the factual basis of such assertion. Absent a proper and timely objection, the person so selected shall act as Independent Counsel. If such written objection is so made and substantiated, the Independent Counsel so selected may not serve as Independent Counsel unless and until such objection is withdrawn or the Delaware Court has determined that such objection is without merit. If, within twenty (20) days after the later of submission by Indemnitee of a written request for indemnification pursuant to Section 11(a) hereof and the final disposition of the Proceeding, no Independent Counsel shall have been selected and not objected to, either the Company or Indemnitee may petition the Delaware Court for resolution of any objection which shall have been made by the Company or Indemnitee to the other's selection of Independent Counsel and/or for the appointment as Independent Counsel of a person selected by such court or by such other person as such court shall designate, and the person with respect to whom all objections are so resolved or the person so appointed shall act as Independent Counsel under Section 12(a) hereof. Upon the due commencement of any judicial proceeding or arbitration pursuant to Section 14(a) of this Agreement, Independent Counsel shall be discharged and relieved of any further responsibility in such capacity (subject to the applicable standards of professional conduct then prevailing).

Section 13. Presumptions and Effect of Certain Proceedings.

(a) In making a determination with respect to entitlement to indemnification hereunder, the person or persons or entity making such determination shall, to the fullest extent not prohibited by law, presume that Indemnitee is entitled to indemnification under this Agreement if Indemnitee has submitted a request for indemnification in accordance with Section 11(a) of this Agreement, and the Company shall, to the fullest extent not prohibited by law, have the burden of proof to overcome that presumption in connection with the making by any person, persons or entity of any determination contrary to that presumption. Neither the failure of the Company (including by its directors or Independent Counsel) to have made a determination prior to the commencement of any action pursuant to this Agreement that indemnification is proper in the circumstances because Indemnitee has met the applicable standard of conduct, nor an actual determination by the Company (including by its directors or Independent Counsel) that Indemnitee has not met such applicable standard of conduct, shall be a defense to the action or create a presumption that Indemnitee has not met the applicable standard of conduct.

(b) Subject to Section 14(e), if the person, persons or entity empowered or selected under Section 12 of this Agreement to determine whether Indemnitee is entitled to indemnification shall not have made a determination within sixty (60) days after receipt by the Company of the request therefor, the requisite determination of entitlement to indemnification

shall, to the fullest extent not prohibited by law, be deemed to have been made and Indemnitee shall be entitled to such indemnification, absent (i) a misstatement by Indemnitee of a material fact, or an omission of a material fact necessary to make Indemnitee's statement not materially misleading, in connection with the request for indemnification, or (ii) a prohibition of such indemnification under applicable law; provided, however, that such 60-day period may be extended for a reasonable time, not to exceed an additional thirty (30) days, if the person, persons or entity making the determination with respect to entitlement to indemnification in good faith requires such additional time for the obtaining or evaluating of documentation and/or information relating thereto; and provided, further, that the foregoing provisions of this Section 13(b) shall not apply (i) if the determination of entitlement to indemnification is to be made by the stockholders pursuant to Section 12(a) of this Agreement and if (A) within fifteen (15) days after receipt by the Company of the request for such determination the Board has resolved to submit such determination to the stockholders for their consideration at an annual meeting thereof to be held within seventy-five (75) days after such receipt and such determination is made thereat, or (B) a special meeting of stockholders is called within fifteen (15) days after such receipt for the purpose of making such determination, such meeting is held for such purpose within sixty (60) days after having been so called and such determination is made thereat, or (ii) if the determination of entitlement to indemnification is to be made by Independent Counsel pursuant to Section 12(a) of this Agreement.

(c) The termination of any Proceeding or of any claim, issue or matter therein, by judgment, order, settlement or conviction, or upon a plea of nolo contendere or its equivalent, shall not (except as otherwise expressly provided in this Agreement) of itself adversely affect the right of Indemnitee to indemnification or create a presumption that Indemnitee did not act in good faith and in a manner which he reasonably believed to be in or not opposed to the best interests of the Company or, with respect to any criminal Proceeding, that Indemnitee had reasonable cause to believe that his conduct was unlawful.

(d) For purposes of any determination of good faith, Indemnitee shall be deemed to have acted in good faith if Indemnitee's action is based on the records or books of account of the Enterprise, including financial statements, or on information supplied to Indemnitee by the directors or officers of the Enterprise in the course of their duties, or on the advice of legal counsel for the Enterprise or on information or records given or reports made to the Enterprise by an independent certified public accountant or by an appraiser or other expert selected with the reasonable care by the Enterprise. The provisions of this Section 13(d) shall not be deemed to be exclusive or to limit in any way the other circumstances in which the Indemnitee may be deemed to have met the applicable standard of conduct set forth in this Agreement.

(e) The knowledge and/or actions, or failure to act, of any director, officer, trustee, partner, managing member, fiduciary, agent or employee of the Enterprise shall not be imputed to Indemnitee for purposes of determining the right to indemnification under this Agreement.

Section 14. Remedies of Indemnitee.

(a) Subject to Section 14(e), in the event that (i) a determination is made pursuant to Section 12 of this Agreement that Indemnitee is not entitled to indemnification under this Agreement, (ii) advancement of Expenses is not timely made pursuant to Section 10 of this

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Agreement, (iii) no determination of entitlement to indemnification shall have been made pursuant to Section 12(a) of this Agreement within ninety (90) days after receipt by the Company of the request for indemnification, (iv) payment of indemnification is not made pursuant to Section 5, 6 or 7 or the last sentence of Section 12(a) of this Agreement within ten (10) days after receipt by the Company of a written request therefor, (v) payment of indemnification pursuant to Section 3, 4 or 8 of this Agreement is not made within ten (10) days after a determination has been made that Indemnitee is entitled to indemnification, or (vi) in the event that the Company or any other person takes or threatens to take any action to declare this Agreement void or unenforceable, or institutes any litigation or other action or Proceeding designed to deny, or to recover from, the Indemnitee the benefits provided or intended to be provided to the Indemnitee hereunder, Indemnitee shall be entitled to an adjudication by a court of his entitlement to such indemnification or advancement of Expenses. Alternatively, Indemnitee, at his option, may seek an award in arbitration to be conducted by a single arbitrator pursuant to the Commercial Arbitration Rules of the American Arbitration Association. Indemnitee shall commence such proceeding seeking an adjudication or an award in arbitration within 180 days following the date on which Indemnitee first has the right to commence such proceeding pursuant to this Section 14(a); provided, however, that the foregoing clause shall not apply in respect of a proceeding brought by Indemnitee to enforce his rights under Section 5 of this Agreement. The Company shall not oppose Indemnitee's right to seek any such adjudication or award in arbitration.

(b) In the event that a determination shall have been made pursuant to Section 12(a) of this Agreement that Indemnitee is not entitled to indemnification, any judicial proceeding or arbitration commenced pursuant to this Section 14 shall be conducted in all respects as a de novo trial, or arbitration, on the merits and Indemnitee shall not be prejudiced by reason of that adverse determination. In any judicial proceeding or arbitration commenced pursuant to this Section 14 the Company shall have the burden of proving Indemnitee is not entitled to indemnification or advancement of Expenses, as the case may be.

(c) If a determination shall have been made pursuant to Section 12(a) of this Agreement that Indemnitee is entitled to indemnification, the Company shall be bound by such determination in any judicial proceeding or arbitration commenced pursuant to this Section 14, absent (i) a misstatement by Indemnitee of a material fact, or an omission of a material fact necessary to make Indemnitee's statement not materially misleading, in connection with the request for indemnification, or (ii) a prohibition of such indemnification under applicable law.

(d) The Company shall, to the fullest extent not prohibited by law, be precluded from asserting in any judicial proceeding or arbitration commenced pursuant to this Section 14 that the procedures and presumptions of this Agreement are not valid, binding and enforceable and shall stipulate in any such court or before any such arbitrator that the Company is bound by all the provisions of this Agreement. It is the intent of the Company that, to the fullest extent permitted by law, the Indemnitee not be required to incur legal fees or other Expenses associated with the interpretation, enforcement or defense of Indemnitee's rights under this Agreement by litigation or otherwise because the cost and expense thereof would substantially detract from the benefits intended to be extended to the Indemnitee hereunder. The Company shall, to the fullest extent permitted by law, indemnify Indemnitee against any and all Expenses and, if requested by Indemnitee, shall (within ten (10) days after receipt by the Company of a written request therefor) advance, to the extent not prohibited by law, such Expenses to Indemnitee, which are incurred by Indemnitee in connection with any action brought by Indemnitee for indemnification or advance

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of Expenses from the Company under this Agreement or under any directors' and officers' liability insurance policies maintained by the Company if, in the case of indemnification, Indemnitee is wholly successful on the underlying claims; if Indemnitee is not wholly successful on the underlying claims, then such indemnification shall be only to the extent Indemnitee is successful on such underlying claims or otherwise as permitted by law, whichever is greater.

(e) Notwithstanding anything in this Agreement to the contrary, no determination as to entitlement of Indemnitee to indemnification under this Agreement shall be required to be made prior to the final disposition of the Proceeding.

Section 15. Non-exclusivity; Survival of Rights; Insurance; Subrogation.

(a) The rights of indemnification and to receive advancement of Expenses as provided by this Agreement shall not be deemed exclusive of any other rights to which Indemnitee may at any time be entitled under applicable law, the Certificate of Incorporation, the Bylaws, any agreement, a vote of stockholders or a resolution of directors, or otherwise. No amendment, alteration or repeal of this Agreement or of any provision hereof shall limit or restrict any right of Indemnitee under this Agreement in respect of any action taken or omitted by such Indemnitee in his Corporate Status prior to such amendment, alteration or repeal. To the extent that a change in Delaware law, whether by statute or judicial decision, permits greater indemnification or advancement of Expenses than would be afforded currently under the Certificate of Incorporation and this Agreement, it is the intent of the parties hereto that Indemnitee shall enjoy by this Agreement the greater benefits so afforded by such change. No right or remedy herein conferred is intended to be exclusive of any other right or remedy, and every other right and remedy shall be cumulative and in addition to every other right and remedy given hereunder or now or hereafter existing at law or in equity or otherwise. The assertion or employment of any right or remedy hereunder, or otherwise, shall not prevent the concurrent assertion or employment of any other right or remedy.

(b) To the extent that the Company maintains an insurance policy or policies providing liability insurance for directors, officers, employees, or agents of the Enterprise, Indemnitee shall be covered by such policy or policies in accordance with its or their terms to the maximum extent of the coverage available for any such director, officer, employee or agent under such policy or policies. If, at the time of the receipt of a notice of a claim pursuant to the terms hereof, the Company has director and officer liability insurance in effect, the Company shall give prompt notice of such claim or of the commencement of a Proceeding, as the case may be, to the insurers in accordance with the procedures set forth in the respective policies. The Company shall thereafter take all necessary or desirable action to cause such insurers to pay, on behalf of the Indemnitee, all amounts payable as a result of such Proceeding in accordance with the terms of such policies.

(c) In the event of any payment under this Agreement, the Company shall be subrogated to the extent of such payment to all of the rights of recovery of Indemnitee, who shall execute all papers required and take all action necessary to secure such rights, including execution of such documents as are necessary to enable the Company to bring suit to enforce such rights.

(d) The Company shall not be liable under this Agreement to make any payment of amounts otherwise indemnifiable (or for which advancement is provided hereunder)

hereunder if and to the extent that Indemnitee has otherwise actually received such payment under any insurance policy, contract, agreement or otherwise.

(e) The Company's obligation to indemnify or advance Expenses hereunder to Indemnitee who is or was serving at the request of the Company as a director, officer, trustee, partner, managing member, fiduciary, employee or agent of any other corporation, limited liability company, partnership, joint venture, trust, employee benefit plan or other enterprise shall be reduced by any amount Indemnitee has actually received as indemnification or advancement of Expenses from such other corporation, limited liability company, partnership, joint venture, trust or other enterprise.

Section 16. Duration of Agreement. This Agreement shall continue until and terminate upon the later of: (a) ten (10) years after the date that Indemnitee shall have ceased to serve as [a][an] [officer][director] of the Company or (b) one (1) year after the final termination of any Proceeding then pending in respect of which Indemnitee is granted rights of indemnification or advancement of Expenses hereunder and of any proceeding commenced by Indemnitee pursuant to Section 14 of this Agreement relating thereto. The indemnification and advancement of expenses rights provided by or granted pursuant to this Agreement shall be binding upon and be enforceable by the parties hereto and their respective successors and assigns (including any direct or indirect successor by purchase, merger, consolidation or otherwise to all or substantially all of the business or assets of the Company), shall continue as to an Indemnitee who has ceased to be a director, officer, employee or agent of the Company or of any other Enterprise, and shall inure to the benefit of Indemnitee and his or her spouse, assigns, heirs, devisees, executors and administrators and other legal representatives.

Section 17. Severability. If any provision or provisions of this Agreement shall be held to be invalid, illegal or unenforceable for any reason whatsoever: (a) the validity, legality and enforceability of the remaining provisions of this Agreement (including without limitation, each portion of any Section of this Agreement containing any such provision held to be invalid, illegal or unenforceable, that is not itself invalid, illegal or unenforceable) shall not in any way be affected or impaired thereby and shall remain enforceable to the fullest extent permitted by law; (b) such provision or provisions shall be deemed reformed to the extent necessary to conform to applicable law and to give the maximum effect to the intent of the parties hereto; and (c) to the fullest extent possible, the provisions of this Agreement (including, without limitation, each portion of any Section of this Agreement containing any such provision held to be invalid, illegal or unenforceable, that is not itself invalid, illegal or unenforceable) shall be construed so as to give effect to the intent manifested thereby.

Section 18. Enforcement.

(a) The Company expressly confirms and agrees that it has entered into this Agreement and assumed the obligations imposed on it hereby in order to induce Indemnitee to serve as a director or officer of the Company, and the Company acknowledges that Indemnitee is relying upon this Agreement in serving as a director or officer of the Company.

(b) This Agreement constitutes the entire agreement between the parties hereto with respect to the subject matter hereof and supersedes and replaces all prior agreements and understandings, oral, written and implied, between the parties hereto with respect to the subject

matter hereof, including any indemnification agreement previously entered into between the Company and the Indemnitee; provided, however, that this Agreement is a supplement to and in furtherance of the Certificate of Incorporation, the Bylaws and applicable law, and shall not be deemed a substitute therefor, nor to diminish or abrogate any rights of Indemnitee thereunder.

Section 19. Modification and Waiver. No supplement, modification or amendment of this Agreement shall be binding unless executed in writing by the parties hereto. No waiver of any of the provisions of this Agreement shall be deemed or shall constitute a waiver of any other provisions of this Agreement nor shall any waiver constitute a continuing waiver.

Section 20. Notice by Indemnitee. Indemnitee agrees promptly to notify the Company in writing upon being served with any summons, citation, subpoena, complaint, indictment, information or other document relating to any Proceeding or matter which may be subject to indemnification or advancement of Expenses covered hereunder. The failure of Indemnitee to so notify the Company shall not relieve the Company of any obligation which it may have to the Indemnitee under this Agreement or otherwise.

Section 21. Notices. All notices, requests, demands and other communications under this Agreement shall be in writing and shall be deemed to have been duly given if (a) delivered by hand and receipted for by the party to whom said notice or other communication shall have been directed, (b) mailed by certified or registered mail with postage prepaid, on the third business day after the date on which it is so mailed, (c) mailed by reputable overnight courier and receipted for by the party to whom said notice or other communication shall have been directed or (d) sent by facsimile transmission, with receipt of oral confirmation that such transmission has been received:

(a) If to Indemnitee, at the address indicated on the signature page of this Agreement, or such other address as Indemnitee shall provide to the Company.

(b) If to the Company, to

Fulcrum Therapeutics, Inc.
26 Landsdowne Street
Cambridge, MA 02139
Attn: Chief Executive Officer

or to any other address as may have been furnished to Indemnitee by the Company.

Section 22. Contribution. To the fullest extent permissible under applicable law, if the indemnification provided for in this Agreement is unavailable to Indemnitee for any reason whatsoever, the Company, in lieu of indemnifying Indemnitee, shall contribute to the amount incurred by Indemnitee, whether for judgments, fines, penalties, excise taxes, amounts paid or to be paid in settlement and/or for Expenses, in connection with any claim relating to an indemnifiable event under this Agreement, in such proportion as is deemed fair and reasonable in light of all of the circumstances of such Proceeding in order to reflect (i) the relative benefits received by the Company, on the one hand, and Indemnitee, on the other hand, as a result of the event(s) and/or transaction(s) giving cause to such Proceeding; and/or (ii) the relative fault of the Company (and its other directors, officers, employees and agents), on the one hand, and Indemnitee, on the other hand, in connection with such event(s) and/or transaction(s).

Section 23. Applicable Law and Consent to Jurisdiction. This Agreement and the legal relations among the parties shall be governed by, and construed and enforced in accordance with, the laws of the State of Delaware, without regard to its conflict of laws rules. Except with respect to any arbitration commenced by Indemnitee pursuant to Section 14(a) of this Agreement, the Company and Indemnitee hereby irrevocably and unconditionally (i) agree that any action or proceeding arising out of or in connection with this Agreement shall be brought only in the Delaware Court, and not in any other state or federal court in the United States of America or any court in any other country, (ii) consent to submit to the exclusive jurisdiction of the Delaware Court for purposes of any action or proceeding arising out of or in connection with this Agreement, (iii) waive any objection to the laying of venue of any such action or proceeding in the Delaware Court, and (iv) waive, and agree not to plead or to make, any claim that any such action or proceeding brought in the Delaware Court has been brought in an improper or inconvenient forum.

Section 24. Identical Counterparts. This Agreement may be executed in one or more counterparts, each of which shall for all purposes be deemed to be an original but all of which together shall constitute one and the same Agreement. Only one such counterpart signed by the party against whom enforceability is sought needs to be produced to evidence the existence of this Agreement.

Section 25. Miscellaneous. Use of the masculine pronoun shall be deemed to include usage of the feminine pronoun where appropriate. The headings of this Agreement are inserted for convenience only and shall not be deemed to constitute part of this Agreement or to affect the construction thereof.

[Remainder of Page Intentionally Left Blank]

IN WITNESS WHEREOF, the parties have caused this Agreement to be signed as of the day and year first above written.

FULCRUM THERAPEUTICS, INC.

INDEMNITEE

By: _____
Name: _____
Title: _____

By: _____
Name: _____
Address: _____

Signature Page to Fulcrum Therapeutics Indemnification Agreement

List of Subsidiaries

Name	Jurisdiction of Incorporation
Fulcrum Therapeutics Securities Corp.	Massachusetts

Consent of Independent Registered Public Accounting Firm

We consent to the reference to our firm under the caption "Experts" and to the use of our report dated May 1, 2019, in the Registration Statement (Form S-1) and related Prospectus of Fulcrum Therapeutics, Inc. dated June 21, 2019.

/s/ Ernst & Young LLP

Boston, Massachusetts
June 19, 2019
