

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

FORM 10-K

- (Mark One)
- ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2020
- OR
- TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 FOR THE
TRANSITION PERIOD FROM TO
Commission File Number 001-38978

FULCRUM THERAPEUTICS, INC.

(Exact name of registrant as specified in its Charter)

Delaware
(State or other jurisdiction of
incorporation or organization)
26 Landsdowne Street
Cambridge, Massachusetts
(Address of principal executive offices)

47-4839948
(I.R.S. Employer
Identification No.)

02139
(Zip Code)

Registrant's telephone number, including area code: (617) 651-8851

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common stock, par value \$0.001 per share	FULC	Nasdaq Global Market

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES NO

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. YES NO

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. YES NO

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). YES NO

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input checked="" type="checkbox"/>	Smaller reporting company	<input checked="" type="checkbox"/>
Emerging growth company	<input checked="" type="checkbox"/>		

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report.

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES NO

As of June 30, 2020, the last business day of the registrant's most recently completed second fiscal quarter, the aggregate market value of the registrant's common stock held by non-affiliates of the registrant, based on the closing price of the shares of common stock on the Nasdaq Global Market on June 30, 2020, was approximately \$239,959,880.

The number of shares of registrant's common stock outstanding as of February 25, 2021 was 32,672,223.

DOCUMENTS INCORPORATED BY REFERENCE

The registrant intends to file a definitive proxy statement pursuant to Regulation 14A relating to the 2021 Annual Meeting of Stockholders within 120 days of the end of the registrant's fiscal year ended December 31, 2020. Portions of such definitive proxy statement are incorporated by reference into Part III of this Annual Report on Form 10-K to the extent stated herein.

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FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements, which reflect our current views with respect to, among other things, our operations and financial performance. All statements other than statements of historical facts contained in this Annual Report on Form 10-K, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth are forward-looking statements. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "might," "outlook," "plan," "potential," "predict," "project," "should," "target," "would," and the negative version of these words and other similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Such forward-looking statements are subject to various risks and uncertainties. Accordingly, there are or will be important factors that could cause actual outcomes or results to differ materially from those indicated in these statements. We believe these factors include but are not limited to those described under the "Risk Factors" section and include, among other things:

- our ongoing clinical trials of losmapimod, including our ongoing Phase 2b and Phase 2 open label clinical trials for the treatment of facioscapulohumeral muscular dystrophy, or FSHD;
- our ongoing Phase 1 clinical trial of FTX-6058 in healthy adult volunteers and our planned clinical trial of FTX-6058 in patients with sickle cell disease, or SCD;
- the impact of the COVID-19 pandemic on our business and operations and our future financial results;
- 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, FTX-6058 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, FTX-6058 and any other product candidates;
- our expectations regarding our ability to fund our operating expenses and capital expenditure requirements with our cash, cash equivalents, and marketable securities;
- 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;
- the progress and results of our collaborations with Acceleron Pharma Inc. and MyoKardia, Inc., a wholly owned subsidiary of Bristol-Myers Squibb Company;
- our ability to identify additional products, product candidates or technologies with significant commercial potential that are consistent with our commercial objectives;
- 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 or a smaller reporting company as defined under the federal securities laws.

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 Annual Report on Form 10-K, 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 Annual Report on Form 10-K and the documents that we have filed as exhibits to Annual Report on Form 10-K 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 Annual Report on Form 10-K are made as of the date of this Annual Report on Form 10-K, 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 Annual Report on Form 10-K 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 Annual Report on Form 10-K 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.

SUMMARY RISK FACTORS

Our business is subject to a number of risks that if realized could materially affect our business, financial condition, results of operations, cash flows and access to liquidity. These risks are discussed more fully in the "Risk Factors" section of this Annual Report on Form 10-K. Our principal risks include the following:

- We have incurred significant losses since our inception. Our net loss was \$70.8 million for the year ended December 31, 2020 and \$82.7 million for the year ended December 31, 2019. We expect to incur losses over the next several years and may never achieve or maintain profitability. As of December 31, 2020, we had an accumulated deficit of \$221.6 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. We expect to devote substantial financial resources to our ongoing and planned activities, particularly as we continue our Phase 2b and Phase 2 open label clinical trials of losmapimod for the treatment of FSHD and continue our recently initiated Phase 1 clinical trial of FTX-6058 in healthy adult volunteers, prepare for our planned clinical trial of FTX-6058 in patients with SCD, and continue research and development and initiate additional clinical trials of, and seek regulatory approval for, these and other product candidates.
- The ongoing COVID-19 pandemic has and may continue to affect our ability to initiate and complete current or future preclinical studies or clinical trials, disrupt regulatory activities or have other adverse effects on our business and operations. In addition, this pandemic may continue to adversely impact economies worldwide, which could result in adverse effects on our business and operations.
- We are early in our development efforts, and we only have two product candidates in clinical trials. 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. 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.
- 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 U.S. Food and Drug Administration 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 rely, and expect to continue 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.
- We have entered into, and may in the future enter into, collaborations with third parties for the discovery, development or commercialization of product candidates, including our collaborations with Acceleron Pharma Inc. and MyoKardia, Inc. 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.
- 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.
- 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.

PART I

Item 1. Business.

Overview

We are a clinical-stage biopharmaceutical company focused on improving the lives of patients with genetically defined rare diseases in areas of high unmet medical need. 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. In August 2019, we initiated a randomized, double-blind, placebo-controlled, multicenter, international Phase 2b clinical trial of losmapimod, our product candidate for FSHD, and a single center, open label Phase 2 clinical trial to investigate the safety and tolerability of chronic treatment with losmapimod in patients with FSHD. The Phase 2b clinical trial and the open label Phase 2 clinical trial completed enrollment in February 2020. In the fourth quarter of 2020, we initiated a Phase 1 clinical trial of FTX-6058, our product candidate for certain hemoglobinopathies and a novel upregulator of fetal hemoglobin, to evaluate the safety, tolerability and pharmacokinetics of FTX-6058 in healthy adult volunteers. In addition, we anticipate initiating a clinical trial of FTX-6058 in patients with SCD in the second half of 2021.

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 and RNAi libraries. We also employ computational biology and FulcrumSeek, our proprietary 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 $p38\alpha/\beta$ mitogen activated protein kinase, or $p38\alpha/\beta$. We utilized our product engine to discover that inhibition of $p38\alpha/\beta$ 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. In January 2020, the U.S. Food and Drug Administration, or FDA, granted orphan drug designation to losmapimod for the treatment of FSHD, and, in March 2020, the European Medicines Agency, or EMA, granted orphan drug designation to losmapimod for the treatment of FSHD.

Following our discovery of the role of $p38\alpha/\beta$ inhibitors in the reduction of *DUX4* expression in patients with FSHD, 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 are conducting a randomized, double-blind, placebo-controlled, multicenter, international Phase 2b clinical trial, referred to as ReDUX4, to investigate whether treatment with losmapimod reduces *DUX4*-driven gene expression in affected skeletal muscle. In this Phase 2b clinical trial, secondary endpoints include evaluation of safety and tolerability in FSHD patients, pharmacokinetic in blood, losmapimod concentration in skeletal muscle biopsies, $p38\alpha/\beta$ target engagement in blood and in muscle biopsies, and efficacy on the whole-body skeletal muscle MRI biomarker. We are concurrently conducting a single center 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 are evaluating the ability of losmapimod to reduce *DUX4*-driven gene expression in affected skeletal muscle over varying treatment durations. We initiated ReDUX4 at multiple sites in the United States, Canada and Europe and the open label Phase 2 clinical trial in Europe in August 2019. We completed dosing in a Phase 1 clinical trial in healthy volunteers and patients with FSHD in September 2019. We presented top-line, blinded results from the Phase 1 clinical trial in October 2019, and we presented unblinded data in March 2020. We utilized data from GSK's clinical trials of losmapimod and our preclinical data to submit an IND, and clinical trial applications, or CTAs, in

Europe and Canada, at various dates during 2019 that have enabled us to advance our clinical development plan for losmapimod in FSHD, including initiating ReDUX4 in August 2019.

As a result of the COVID-19 pandemic, we extended the ReDUX4 treatment period from 24 to 48 weeks through a protocol amendment to ensure the safety of the subjects and to allow for the opportunity for a biopsy at week 16 as originally intended or at week 36. Approximately 64 subjects who did not complete the original 24-week treatment period continued in the 48-week treatment period in the randomized portion of the trial. The extension from 24 to 48 weeks also allows for a longer assessment in a placebo-controlled design of the skeletal muscle MRI secondary endpoint and the various exploratory clinical endpoints, such as reachable workspace, optimized time up and go test for FSHD, muscle function measures and patient reported outcomes. We expect to present full data from the trial in the second quarter of 2021. We believe that the amendment to the trial protocol provides flexibility to address the challenges presented by the COVID-19 pandemic and supports collection of efficacy and safety data to support continued discussions with regulatory agencies regarding potential registration strategies.

In August 2020, we announced results from a pre-specified interim analysis of the primary endpoint of the ReDUX4 trial, which is the reduction from baseline of DUX4-driven gene expression in affected skeletal muscle after subjects have been treated with losmapimod or placebo.

We are additionally conducting several preparatory non-drug studies to assess biomarker endpoints and clinical outcome assessments and are participating in a natural history study that will follow 160 subjects with FSHD in the United States and 60 subjects in Europe over 18 months. We are using data generated to date, and expect to utilize data to be generated from our ongoing 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 to date, and additional data to be generated from our ongoing ReDUX4 trial, may enable us to apply for accelerated approval of losmapimod for the treatment of FSHD. If we observe positive results in ReDUX4 based on our biomarker efficacy endpoint of reduction in DUX4-driven gene expression in affected skeletal muscle, we plan to discuss the possibility of applying for accelerated approval with regulatory agencies and may seek accelerated approval if such regulatory agencies believe 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.

In June 2020, we announced that we received notification from the FDA that we may proceed with initiating a Phase 3, randomized, double-blind, placebo-controlled trial of losmapimod in higher risk hospitalized adults with COVID-19, or the LOSVID trial. The LOSVID trial is a Phase 3, international, multicenter trial designed to assess the safety and efficacy of a 15 mg twice per day oral dose of losmapimod compared to placebo for 14 days on top of standard of care in approximately 400 patients hospitalized with COVID-19 and at risk of progression to critical illness based on older age and elevated systemic inflammation. We began enrolling patients in the fourth quarter of 2020. The primary endpoint of the trial is the proportion of patients who progress to death or respiratory failure by day 28. The trial's secondary endpoints include clinical status on days seven and 14 as measured on the nine point World Health Organization ordinal scale of COVID-19 severity, total number of study days free of oxygen supplementation, all-cause mortality, length of hospitalization and intensive care unit stay, adverse events and viral clearance. In March 2021, we announced the discontinuation of the LOSVID trial following a strategic review.

Our second product candidate, FTX-6058, is our novel small molecule designed to bind embryonic ectoderm development, or EED, and inhibit the transcriptional silencing activity of the polycomb repressive complex 2, or PRC2. FTX-6058 is a small molecule designed to upregulate fetal hemoglobin in patients with SCD and β -thalassemia. SCD is a genetic blood disorder caused by a mutation in the β -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. β -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-6058 to compensate for the root cause of these hemoglobinopathies by inducing the expression of the two γ -globin genes, *HBG1/2*, whose expression is normally silenced shortly after birth. The *HBG1/2* genes encode for γ -globin, a component of fetal hemoglobin, which is known to compensate for the presence of abnormal hemoglobin in SCD and β -thalassemia. We have observed *in vitro* and *in vivo* activation of the *HBG1/2* genes in preclinical studies with FTX-6058. We have also observed that FTX-6058 demonstrated robust levels of fetal hemoglobin elevation with no adverse effect on important cellular health markers. We conducted additional pre-clinical profiling in CD34+ derived cells and observed that treatment with FTX-6058 increased HbF levels to approximately 30% of total hemoglobin, as measured by mass

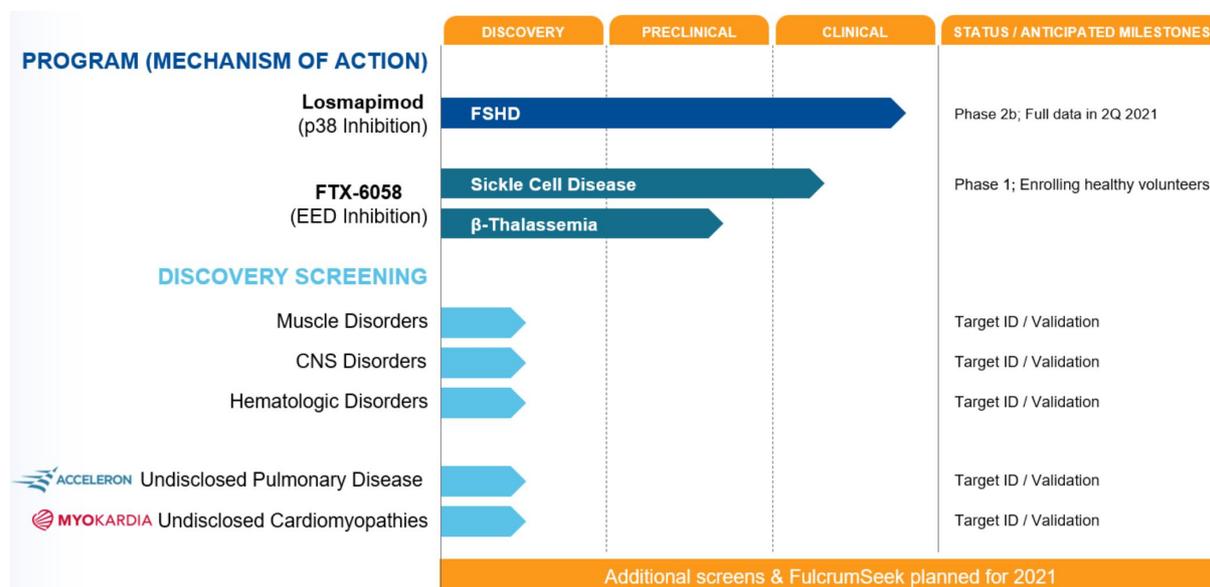
spectrometry, high performance liquid chromatography, and fast protein liquid chromatography techniques. The elevation of HbF was significantly greater than we observed with hydroxyurea in the cell models.

In the fourth quarter of 2020, we initiated our Phase 1 clinical trial of FTX-6058 in healthy adult volunteers. In this trial, we are evaluating the safety, tolerability and pharmacokinetics of FTX-6058. The trial is comprised of four parts. Part A is a randomized, double-blind, placebo-controlled, single ascending dose study in up to six cohorts. Part B is a randomized, double-blind, placebo-controlled, multiple ascending dose study in up to four cohorts dosed once daily for 14 days. Part C is an open label pilot food effect study in subjects randomized to take FTX-6058 with and without a high-fat meal, and Part D is an open label study to evaluate the potential of FTX-6058 to induce a liver enzyme known as CYP3A, which is involved in drug metabolism. We expect to present data from the Phase 1 clinical trial in mid-2021. In addition, we anticipate initiating a clinical trial of FTX-6058 in patients with SCD in the second half of 2021.

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. Our current drug target identification and development efforts are focused on rare neuromuscular, muscular, hematologic and central nervous system, or CNS, disorders. We also anticipate utilizing our product engine to discover drug targets for genetically defined diseases in other therapeutic areas and for other disorders. 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. For example, we are utilizing our product engine to discover drug targets within a targeted indication within the pulmonary disease space under our collaboration and license agreement with Acceleron Pharma Inc., or Acceleron, and for the potential treatment of certain genetically defined cardiomyopathies under our collaboration and license agreement with MyoKardia, Inc., or MyoKardia, a wholly owned subsidiary of Bristol-Myers Squibb Company.

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 Strategy

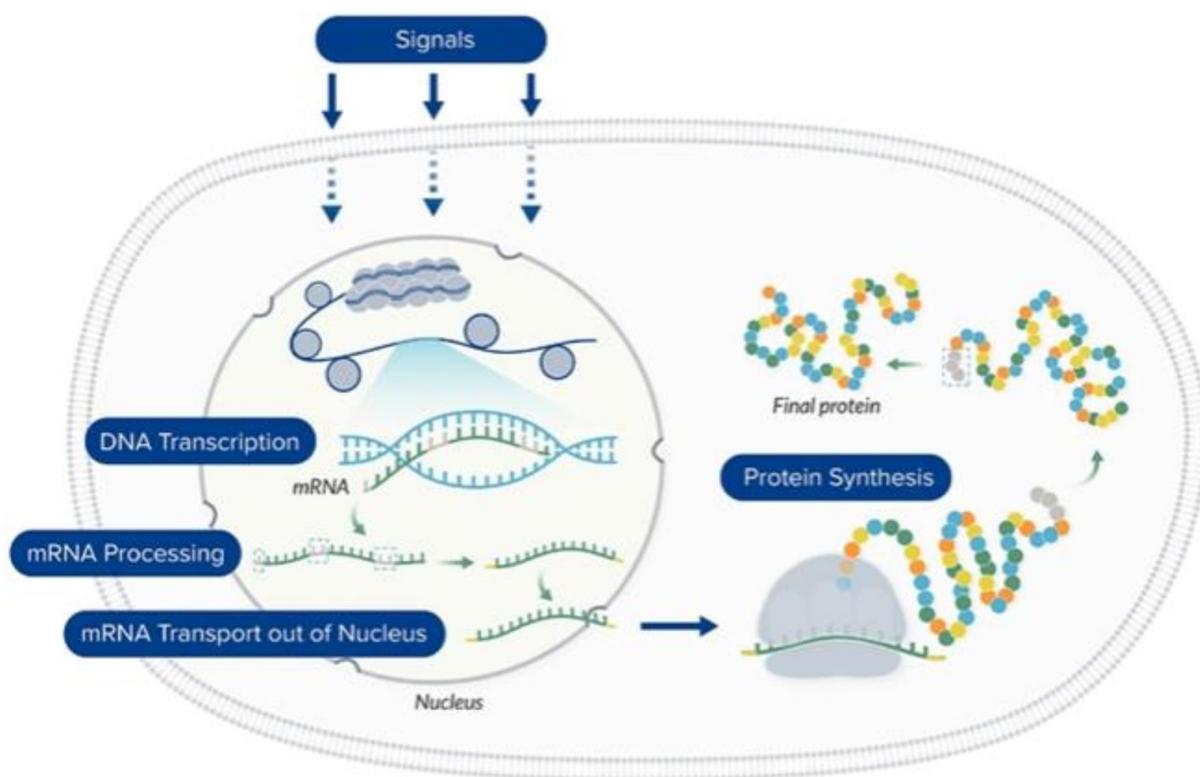
We are leveraging the broad applicability of our proprietary product engine to discover and develop small molecule therapies that modulate gene expression to address the known root cause of genetically defined rare diseases in areas of high unmet medical need. We believe that our initial product candidates 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 and novel 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 initiated a randomized, double-blind placebo-controlled multicenter international Phase 2b clinical trial of losmapimod, or ReDUX4, in August 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.
- **Rapidly develop FTX-6058 for the treatment of select hemoglobinopathies.** We have initiated a Phase 1 clinical trial of FTX-6058 in healthy adult volunteers and, subject to positive results, plan to initiate a clinical trial of FTX-6058 in patients with SCD in the second half of 2021.
- **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 disease.
- **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 or RNAi 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 for such rare genetically defined diseases 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, such as our collaboration and license agreements with Acceleron and MyoKardia. 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, muscular, hematologic and CNS disorders. 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 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 or RNAi libraries across healthy and diseased human cells, such as skeletal muscle cells, cardiac muscle cells, brain cells and blood cells. Our FulcrumSeek database is designed to provide a unique understanding into gene regulatory and signaling pathways that may be relevant for the activation or repression of a particular gene associated with the disease of interest. To achieve this, we profile many features that are impacted when a cell of interest is treated with a perturbagen, such as a small molecule probe, CRISPR guide, small interfering RNA, or microRNAs. These features include a comprehensive assessment of transcripts that are modulated (quantified by RNA sequencing, or RNAseq) and cellular processes that are measured by imaging techniques. We expect that the data from these screens will 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. Moreover, with the initiation of our collaborations with Acceleron and MyoKardia, we are further demonstrating the scope of our disease modeling and target identification capabilities with the expansion into pulmonary and cardiovascular disease.

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 mining our FulcrumSeek database or screening with our proprietary small molecule library and customized CRISPR or RNAi 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.

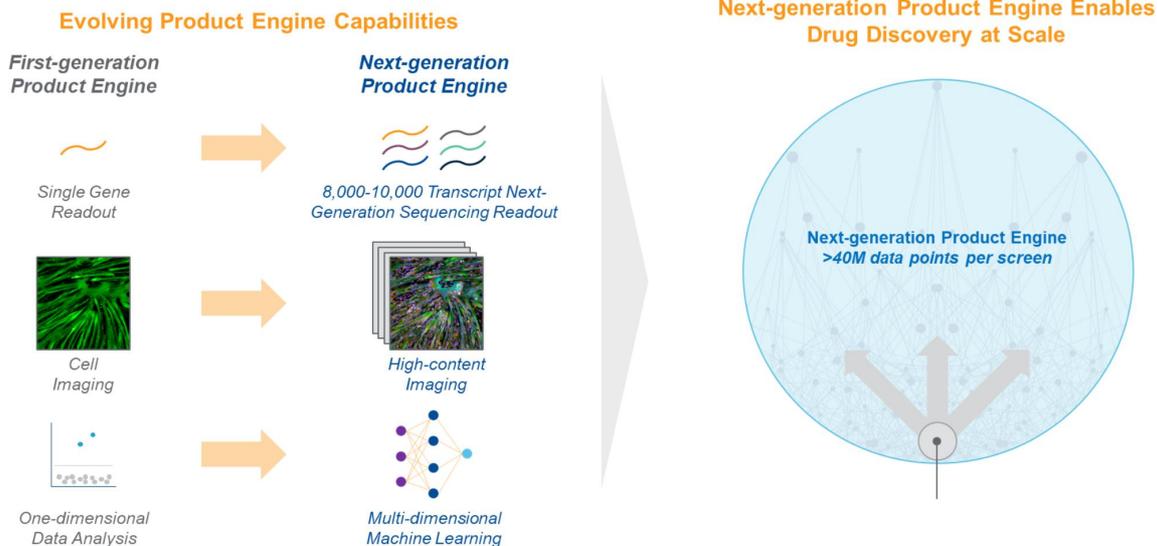
Our product engine is designed to enable us to address diseases in which genes are mis-expressed, silenced or result in mutated gene products, such as RNA or protein, due to an underlying genetic defect. There are varied approaches to treating disease by balancing gene expression including reducing the expression of a gene that causes disease (*e.g.*, *DUX4* in FSHD), increasing the expression of an under-expressed gene or expressing a compensatory gene (*e.g.*, *HBG1/2* in SCD and β -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

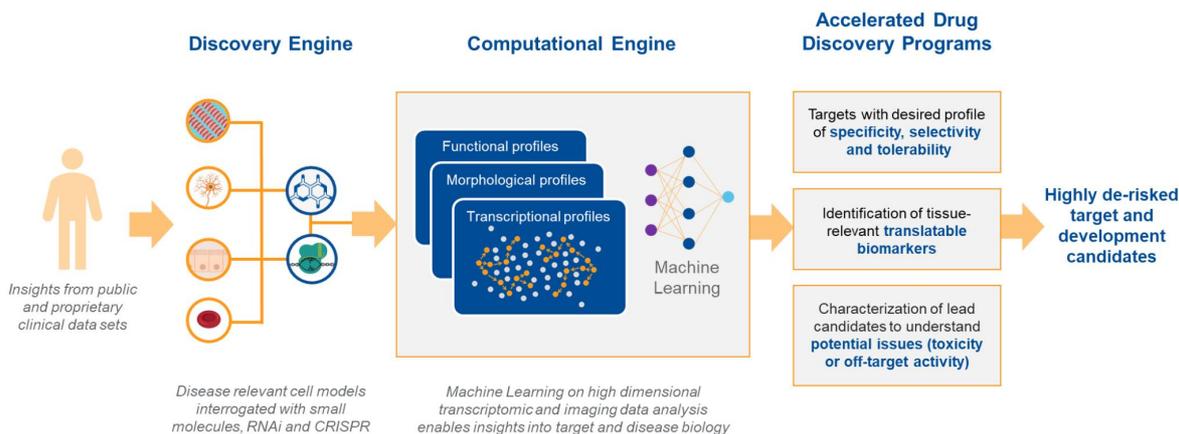
Our product engine is a high-throughput discovery platform that we designed to identify and validate drug targets that balance the expression of the genes known to drive or ameliorate root cause biology. We obtain patient-derived, tissue-relevant cell lines or other relevant human cell lines. We then differentiate these cell lines into those most relevant for the disease pathology, including skeletal muscle myotubes, cardiomyocytes, neurons, RBCs, or other cell lines of interest, 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 or RNAi libraries to the cells to assess for the desired modulation. We have continued to build our capabilities to maximally profile changes in transcription that occur when relevant cells are treated with small molecules or genetic reagents. In addition to profiling a specific gene of interest, we can evaluate multiple genes of potential interest through multiplexed transcriptome profiling to assess effects on root cause biology. FulcrumSeek is a further expansion of this concept, where thousands of transcripts can be measured, and additional features of cellular health and function can be assessed using high-throughput imaging techniques. Our screening approach, coupled with data mining of FulcrumSeek, is the basis of our target identification strategy. 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, such as machine learning algorithms, 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. The first-generation of our product engine was focused on single gene readouts, simple immunocytochemistry, and one-dimensional data analysis focused on an individual gene of interest. With continued investment in the product engine, we have enabled our next-

generation product engine which utilizes RNAseq, high-content imaging, and machine learning. We believe that this next-generation product engine enables 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.



Importantly, we designed our next-generation product engine to iteratively and systematically explore disease or indication areas of interest by incorporating both preclinical and clinical data related to potential drug targets. In the case of heterogeneous diseases, this iterative and systematic approach enables us to explore diseases with less defined root cause genes, and instead screen for targets that modulate root cause biology. This approach not only enables us to validate the translatability of our preclinical models to the clinic, but also enables us to generate unique clinical biology insights utilizing public and proprietary clinical datasets, that can be further queried by our FulcrumSeek database or incorporated into our preclinical disease models. As a result, we believe that our next-generation product engine greatly expands the number of diseases that we can potentially interrogate using our screening approach.

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 genes 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 6,000 small molecules relating to approximately 2,500 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.

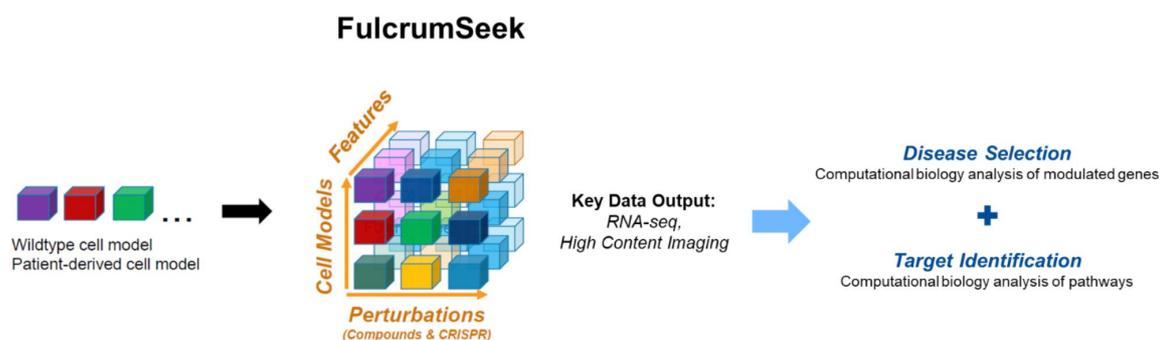
Genetic Screening

We may also use a customized CRISPR or RNAi 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 and RNAi 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. Additionally, we utilize RNAi libraries where CRISPR libraries cannot be employed in the cell type of interest. Specific targets that modulate the gene of interest can be identified via CRISPR or RNAi 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

FulcrumSeek is our proprietary database containing profiles of the effect of perturbagens, or disruptions to cellular processes, on disease-relevant, human derived cell systems. The features captured in this database consist of measures of gene regulation on thousands of genes, and other important assessments of cellular function and health. 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. We can use FulcrumSeek to aid in the selection of diseases that we may want to consider for a discovery program. Our database and analysis can provide information as to which genes are modulated by our perturbagens and which genes may be difficult to modulate. This information is then integrated into our decision-making process for disease selection. Using FulcrumSeek, 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 modulate the root cause gene or root cause biology 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 p38 α / β 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.

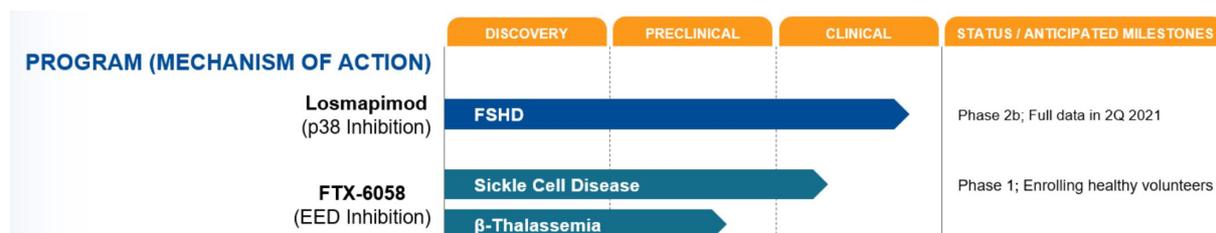
Advantages of a Small Molecule Approach

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 disorders 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. The following chart summarizes key information about our lead product candidates.



Our Product Candidate for Facioscapulohumeral Muscular Dystrophy

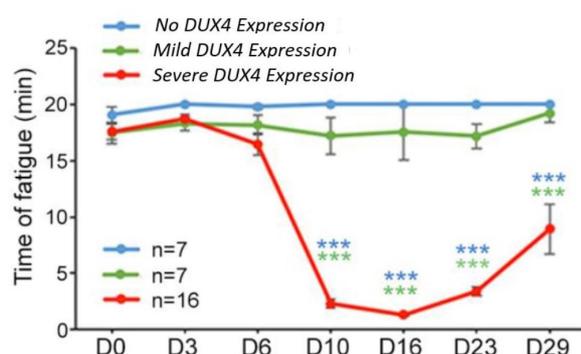
Overview of Facioscapulohumeral Muscular Dystrophy

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.

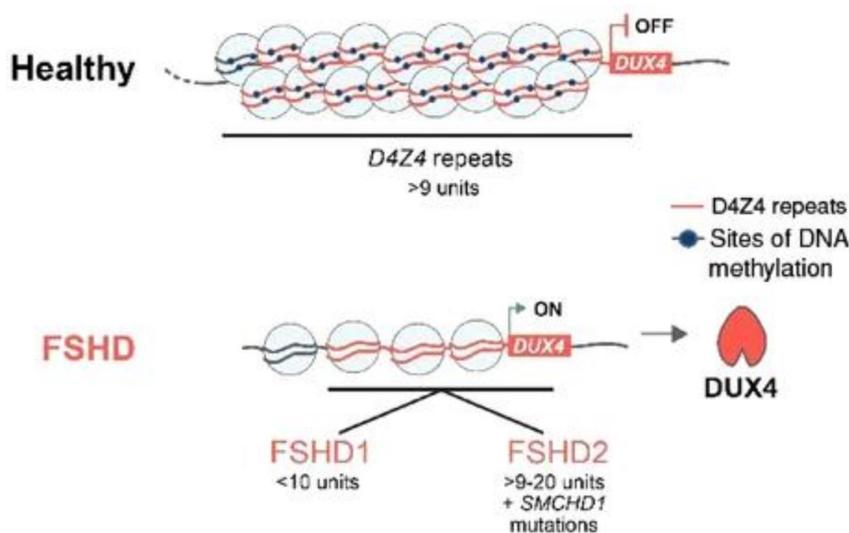
FSHD Biology

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. 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. Published preclinical and human data, in addition to *in vitro* experiments that we have conducted, suggest that any reduction in DUX4 expression may be beneficial for patients. In preclinical studies, we have demonstrated that there is a direct relationship between muscle cell death (apoptosis) and the level of DUX4 expression, and a reduction in DUX4 leads to a concomitant decrease in apoptosis. As illustrated in the graphic below, in animal models where expression of DUX4 in skeletal muscle is induced, a corresponding loss of function is observed with increasing levels of DUX4 expression. In these animal models where low levels of DUX4 are expressed, the animals performed similarly to healthy animals in a mobility assessment, suggesting that complete DUX4 reduction is not required for a functional benefit. Data from human muscle biopsies likewise indicated that increased DUX4 activity is related to worsening muscle pathology.



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 (FSD2) result in aberrant expression of *DUX4* in skeletal muscle.



Our Product Engine Identified the Drug Target for FSHD

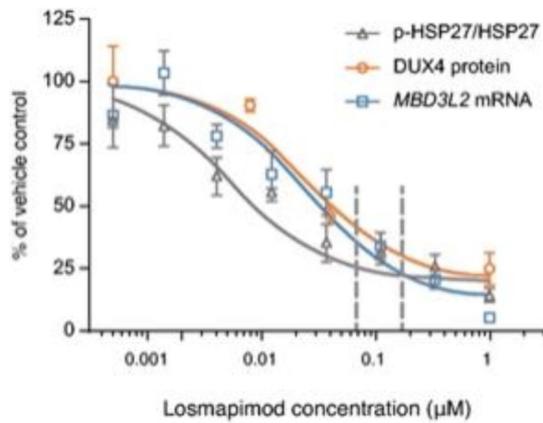
We utilized patient-derived FSHD1 muscle cells, known as myotubes, and screened them with our small molecule probe library to identify drug targets that reduced *DUX4* expression. We identified several potential drug targets, however the modulation of the majority of the targets adversely affected the 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 p38 α / β , 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 p38 α / β inhibitors and observed a consistent reduction of both *DUX4* expression and *DUX4*-driven gene transcripts with each p38 α / β inhibitor. We conducted further validation experiments to confirm that inhibition of p38 α using genetic approaches such as siRNA and CRISPR single-guide RNAs, also led to a reduction in *DUX4* expression. Additionally, researchers from Saint Louis University independently published the results of a study which concluded that inhibitors of p38 α / β , including losmapimod, suppressed *DUX4* expression in cellular and animal FSHD models.

Losmapimod

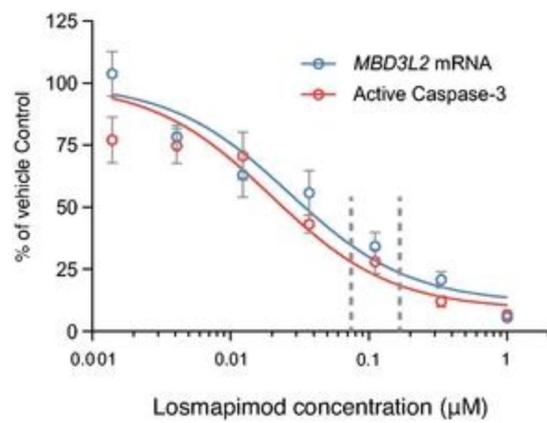
After identifying p38 α / β as a potential drug target, we evaluated multiple small molecule inhibitors of p38 α / β . Each of these inhibitors had previously been evaluated in clinical trials for the treatment of various diseases but never in muscle disorders. As a result of our evaluation and relative to other p38 α / β 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 p38 α / β 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 p38 α / β 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 p38 α / β 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.

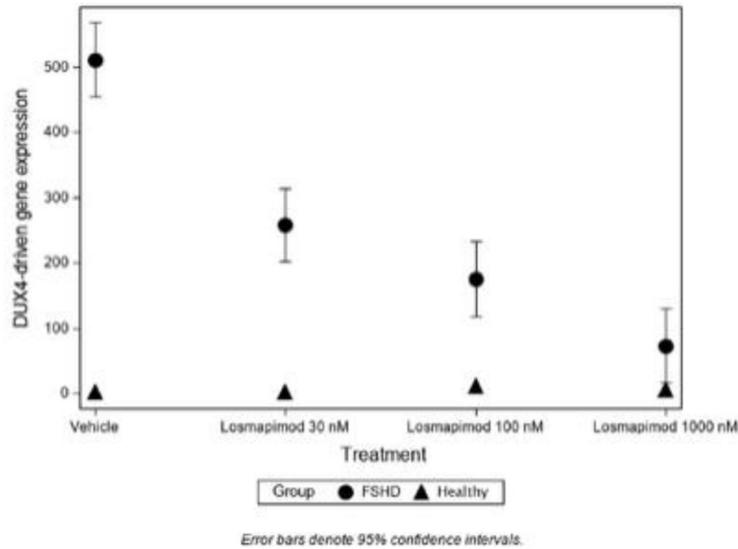
After identifying losmapimod, we in-licensed the molecule from GSK because we believed that its safety and pharmacology history would significantly expedite our development plan and enhance our future regulatory submissions. In February 2019, we obtained an exclusive worldwide license from GSK to the losmapimod patents and preclinical and clinical data for all indications, subject to certain conditions. This license includes a letter of reference for the 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 are using the API and tablets to support our clinical development of losmapimod in FSHD, including our ongoing 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 at various dates during 2019, which enabled us to advance our clinical development plan for losmapimod in FSHD, including initiating our randomized, double-blind placebo-controlled multicenter international Phase 2b clinical trial, or ReDUX4, and a single center Phase 2 open label trial in August 2019. The Phase 2b clinical trial and open label Phase 2 clinical trial completed enrollment in February 2020.

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.

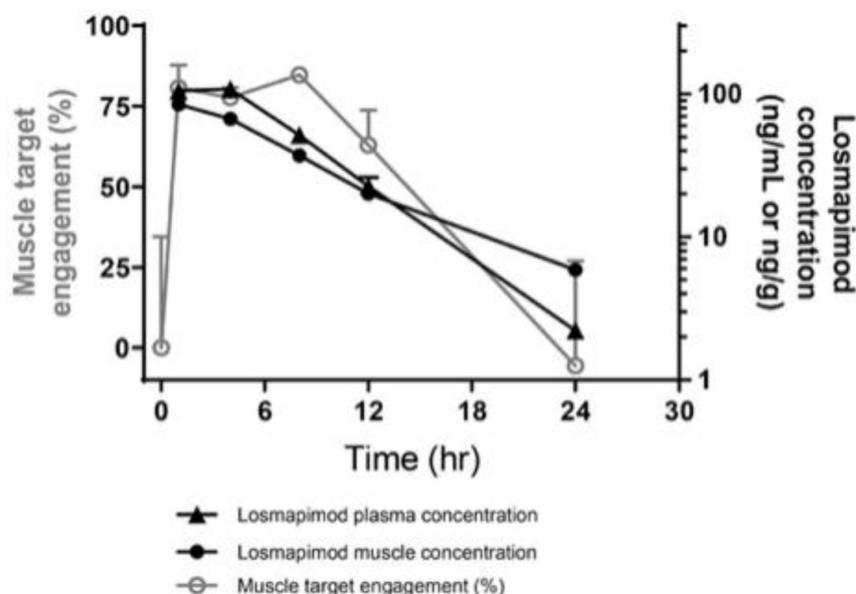
Reduction of DUX4-driven gene expression at increasing concentrations of losmapimod



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.

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 p38 α / β 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.

p38 α / β 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 adult volunteers and patients with FSHD in Europe in February 2019 following the filing of a CTA in December 2018. We completed dosing in this trial in September 2019. In August 2019, we initiated a randomized, double-blind placebo-controlled multicenter international Phase 2b clinical trial, ReDUX4, with 80 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. In August 2019, we also initiated a single center open label Phase 2 clinical trial in up to 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. In addition, in February 2020 we initiated an open label extension of the ReDUX4 trial to enable patients in our ongoing Phase 2b clinical trial who are treated with losmapimod to continue receiving treatment after the 24-week or 48-week treatment period and to enable patients given placebo in our Phase 2b clinical trial to be treated with losmapimod.

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 p38 α / β target engagement data generated by GSK and p38 α / β target engagement data from our preclinical studies. Results of PK in blood and losmapimod concentrations in skeletal muscle and target engagement in blood from the Phase 1 clinical trial in FSHD patients support the selection of the 15 mg twice per day dose of losmapimod for the ongoing Phase 2 clinical trials.

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 at various dates during 2019. Each of the CTAs have been accepted.

The original design of ReDUX4 included a muscle biopsy at week 16 during the 24-week treatment period followed by an open label extension. Sixteen of the 80 subjects in trial have completed the 24-week treatment period and rolled over to the open label extension portion of the trial. As a result of the COVID-19 pandemic, we extended the ReDUX4 treatment period from 24 to 48 weeks through a protocol amendment to ensure the safety of the subjects and to allow for the opportunity for a biopsy at week 16 as originally intended or at week 36. Approximately 64 subjects who did not complete the original 24-week treatment period continued in the 48-week treatment period in the randomized portion of the trial. The extension from 24 to 48 weeks also allows for a longer assessment in a placebo-controlled design of the skeletal muscle MRI secondary endpoint and the various exploratory clinical endpoints, such as reachable workspace, optimized time up and go test for FSHD, muscle function measures and patient reported outcomes. We expect to present full data from the trial in the second quarter of 2021. We believe that the amendment to the trial protocol provides flexibility to address the challenges presented by the COVID-19 pandemic and supports collection of efficacy and safety data to support continued discussions with regulatory agencies regarding potential registration strategies.

In August 2020, we announced results from a pre-specified interim analysis of the primary endpoint of the ReDUX4 trial, which is the reduction from baseline of DUX4-driven gene expression in affected skeletal muscle after subjects have been treated with losmapimod or placebo. Secondary and exploratory endpoints were not assessed as part of this analysis. Results from the interim analysis in the first 29 randomized subjects indicate that DUX4-driven gene expression did not show a separation from placebo at 16 weeks. However, in a pre-specified sensitivity analysis, those with the highest pre-treatment DUX4-driven gene expression in their muscle biopsy sample showed a large reduction in DUX4-driven gene expression following treatment with losmapimod compared to placebo. The highest expressing muscle biopsies represent the top quartile of biopsies assessed based on baseline DUX4-driven gene expression.

The interim results included an analysis of the first 29 subjects who completed their 16-week biopsy out of the 80 subjects enrolled. Pharmacokinetics, demographics and the primary endpoint were assessed. The interim analysis was not powered for statistical significance and did not include individual patient level data. Subjects were randomized to receive an oral dose of losmapimod 15mg (n=15) or placebo (n=14) twice per day. While results showed a significant reduction in DUX4-driven gene expression in the muscle biopsies of subjects whose baseline biopsy showed the highest levels of DUX4 gene expression (38-fold decrease with losmapimod, n=3, and 5.4 fold-decrease with placebo, n=5), the population level data analysis of the reduction in DUX4-driven gene expression from all 29 subjects did not show a separation of losmapimod from placebo (3.7 fold increase with losmapimod, n=15, and 2.8 fold increase with placebo, n=14). Results indicated that muscle biopsies within the higher range of DUX4-driven gene expression at baseline may be needed to observe a reduction.

We believe that the safety data from GSK's prior losmapimod clinical trials, together with safety and efficacy data from our Phase 1 and ongoing 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 are also conducting or have completed, several preparatory non-drug studies to assess biomarker endpoints and clinical outcome assessments. In addition, we are participating in a natural history study that plans to follow 160 subjects with FSHD in the United States and 60 subjects in Europe over 18 months. Planned enrollment in this study was completed in December 2019. We are using data generated to date, and expect to utilize data generated in the future, from our non-drug studies and the natural history study to inform discussions with regulatory agencies and future clinical trial design.

In January 2020, the FDA granted orphan drug designation to losmapimod for the treatment of FSHD. In March 2020, the EMA granted orphan drug designation to losmapimod for the treatment of FSHD.

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 p38 α / β 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 p38 α / β 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 one ongoing and three completed preparatory non-drug studies designed to inform molecular and imaging biomarker and clinical development efficacy endpoints for ongoing clinical trials of losmapimod in patients with FSHD.

Study	Subjects (Planned, for ongoing studies)	Description / Endpoints	Status
Biomarker Preparatory Study (Fulcrum SRA 002-2018)	17	DUX4-driven gene expression in skeletal muscle and whole-body skeletal muscle MRI	Completed
Optimized Time Up and Go Test Preparatory Study (Fulcrum SRA 003-2018)	22	Optimized time up and go test for FSHD, or FSHD-TUG	Completed
Direct Patient Input (Fulcrum SRA 004-2018)	79	Direct patient input into the Phase 2b clinical trial	Completed
ReSOLVE Natural History Study (NIH) and Reachable Work Space (Fulcrum SRA 003-2017)	160	Natural history study Reachable work space	Ongoing
EU Natural History Study and Reachable Work Space (SRA 003- 2017)	60	Natural history study Reachable work space	Ongoing

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 are currently in use in Phase 2 clinical trials of losmapimod for the treatment of FSHD. We enrolled and evaluated 17 subjects at seven clinical sites.

This preparatory study was 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. Based on the results of this study, we believe that the DUX4-driven gene transcript 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 infiltration and replacement 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.

We also are using other MRI-based measures as secondary endpoints in our ongoing Phase 2 clinical trials of losmapimod. We believe that muscle pathology in skeletal muscles of patients with FSHD is predictive of muscle degradation and subsequent fat replacement. We are utilizing MRI-based endpoints to identify the level of muscle pathology and the overall fat content in muscles. MRI imaging sequences, which are settings of pulses and gradients, have been developed that enable an increased contrast between tissues of interest. We use a T2 MRI sequence to observe and quantify areas of high muscle water content, or muscle edema, which is a marker of muscle pathology. These areas have a higher T2 value than the background tissue. T2 provides information about the muscle's physiological status, however it is not specific for muscle edema and may indicate other abnormal conditions in muscle tissue. We are using the Dixon MRI sequence, or the Dixon method, to quantify the fat content of muscles, which is a marker for muscle degradation. The Dixon method separates the signals from water and fat and the separated fat signal can then be utilized to determine the fat infiltration and fraction within the muscle. We are using these MRI-based approaches as additional efficacy endpoints in our Phase 2 open label trial and Phase 2b clinical trial to identify muscles with higher levels of muscle pathology for muscle biopsy, as evidenced by a higher signal in the T2 sequence, and muscle degradation, as evidenced by intermediate levels of muscle fat fraction determined using the Dixon method.

A third-party study found that these MRI techniques, when applied to FSHD skeletal muscles, were able to quantify the increase in muscle pathology, as measured by fat fraction, as determined using the Dixon method, over a 20-month period. In particular, skeletal muscles with severe muscle pathology, as determined by elevated T2 signal, demonstrated progressive worsening of fat fraction over this period. This effect was observed as early as six months. Skeletal muscles in patients with FSHD that had low muscle pathology, based on a low T2 signal, demonstrated both lower levels of fat fraction and slower fat fraction progression. We believe that these data suggest that fat fraction progression is higher in muscles with a higher level of muscle pathology as measured by T2, and support the usage of these MRI-based endpoints in our ongoing clinical trials of losmapimod for the treatment of FSHD.

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

We evaluated 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 tested 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 had clinical severity scores of one to four on the Ricci scale. We evaluated the subjects in five visits over approximately 12 months. In addition, 10 of these subjects were enrolled in a three-month sub-study to assess mobility at home using a touchless sensor and machine learning platform for health analytics. We believe that this sub-study will provide valuable information regarding how measures of mobility conducted during clinical visits compare to mobility in every-day setting in subject's homes. We are analyzing the data from these studies to inform our ongoing Phase 2 trials of losmapimod for the treatment of FSHD.

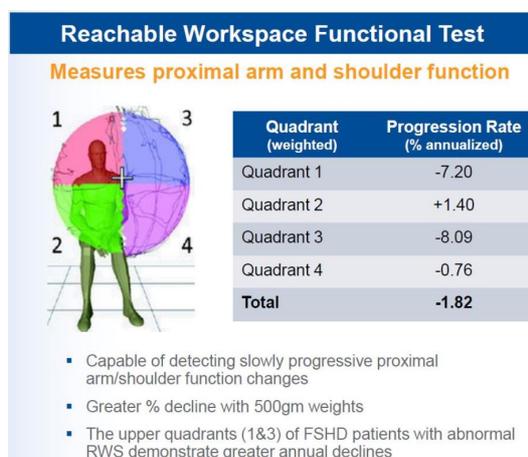
Direct Patient Input (Fulcrum SRA 004-2018)

We also obtained direct patient input into the design and feasibility of our Phase 2b clinical trial by having 79 patients with FSHD complete a survey based on their review of the proposed schedule of clinical assessments for the trial. The patients provided their views on their willingness to participate and any potential barriers to their participation in our then-planned Phase 2b clinical trial. We conducted 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. This survey study provided us with the ability to refine the protocol for our ongoing Phase 2b clinical trial, if needed, and to inform the design of the long-term open label extension of the ReDUX4 trial to reflect the feedback from patients.

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 up to 160 subjects for 24 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 60 subjects for 24 months. 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. Furthermore, the RWS assessment has been registered as medical device in the U.S., Canada and Europe.

A recent third-party study assessed changes in RWS for 18 subjects with FSHD for up to five years. As illustrated in the figure below, the study concluded that the RWS measure is able to detect slow declines in upper extremity function in subjects with FSHD as early as 1 year. The study also found that the most notable declines in RWS were in above-the-shoulder level quadrants with no significant changes in lower quadrants and that RWS declined more significantly if the subjects wore 500-gram weights on their wrists.

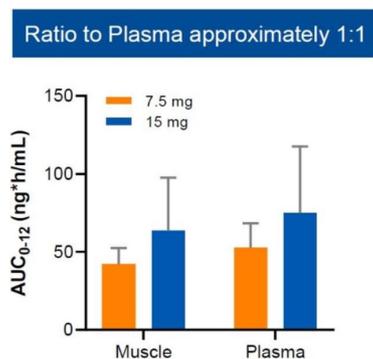


Clinical Trial: Phase 1

We conducted 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. The primary objective of the trial was to investigate the safety and tolerability of losmapimod in healthy volunteers and in FSHD patients. The secondary objective was to evaluate repeated dose PK, and target engagement in FSHD patients in blood and muscle. This trial completed dosing in September 2019 and we presented unblinded data in March 2020.

In the first cohort, 10 healthy volunteers were randomized to a single oral dose of 7.5 mg of losmapimod (n=8) followed by a single oral dose of 15 mg after a wash out period or to single oral dose placebo (n=2) in both dosing periods. In the second cohort, 15 FSHD patients were randomized and treated with placebo (n=3) or 7.5 mg of losmapimod (n=6) or 15 mg of losmapimod (n=6) taken orally twice daily for 14 days. The third cohort was open label with five FSHD patients treated with 15 mg of losmapimod twice daily for 14 days. Biopsies of normal appearing (second cohort) and actively involved (STIR+) muscle (third cohort) were performed at baseline and during treatment.

Losmapimod was well tolerated with no serious adverse events reported. Similar tolerability, safety and PK were observed in healthy volunteers and patients with FSHD. Treatment with losmapimod demonstrated dose-dependent PK and target engagement in blood. FSHD patients treated with losmapimod also achieved dose-dependent concentrations in skeletal muscle, with a muscle to plasma exposure ratio of approximately 1:1. Evidence of dose-dependent target engagement was also observed in skeletal muscle. The losmapimod 15 mg dose taken orally twice daily demonstrated sustained drug concentrations that in preclinical models with human FSHD myotubes resulted in a robust reduction of DUX4-driven gene expression. These data support the selection of the 15 mg dose of losmapimod taken orally twice daily in our ongoing Phase 2b placebo-controlled clinical trial and Phase 2 open label clinical trial of losmapimod.



We manufactured the losmapimod capsules for this trial prior to our license agreement with GSK. For our ongoing Phase 2 clinical trials, we are using 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. We also confirmed that the p38 α / β target engagement in blood from our losmapimod capsules is consistent with the previous data on target engagement of the losmapimod tablets manufactured by GSK.

Clinical Trial: Phase 2b (ReDUX4)

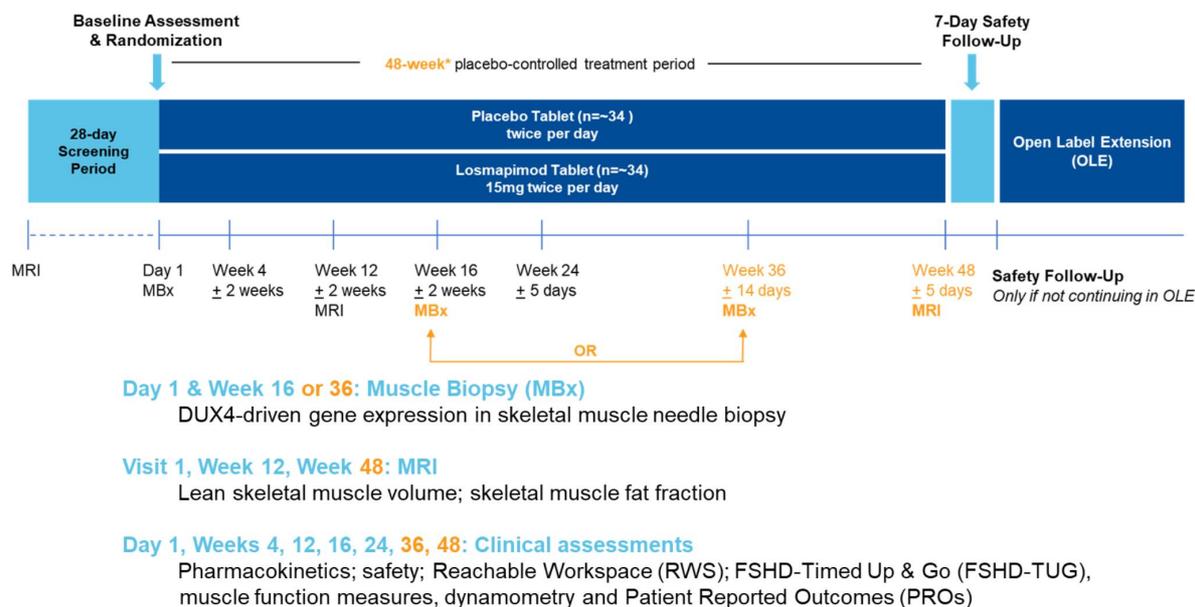
In August 2019, we initiated a randomized, double-blind, placebo-controlled multicenter international Phase 2b clinical trial in 80 patients with FSHD1 and clinical severity scores of two to four on the Ricci scale. In this trial, we are evaluating treatment with 15 mg of losmapimod or placebo tablets twice per day over a 24 or 48-week period. Enrollment was completed in February 2020. Patients were randomized 1:1 between the treatment and placebo arms. The FDA accepted the IND for losmapimod in June 2019, and we also submitted CTAs at various dates during 2019 to conduct the trial at sites in Europe and Canada, all of which were accepted.

The primary endpoint is the reduction of DUX4-driven gene expression in affected skeletal muscle biopsies before treatment and after approximately 16 weeks or 36 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 include evaluation of safety and tolerability in FSHD patients, PK in blood, losmapimod concentration in skeletal muscle biopsies, p38 α / β target engagement in blood and in muscle biopsies, and efficacy on the whole-body skeletal muscle MRI biomarker. This trial also includes evaluation of exploratory efficacy endpoints including 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.

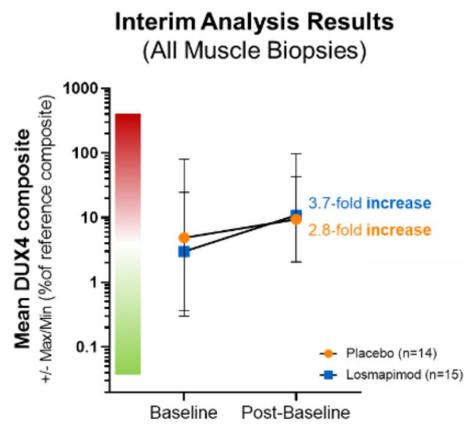
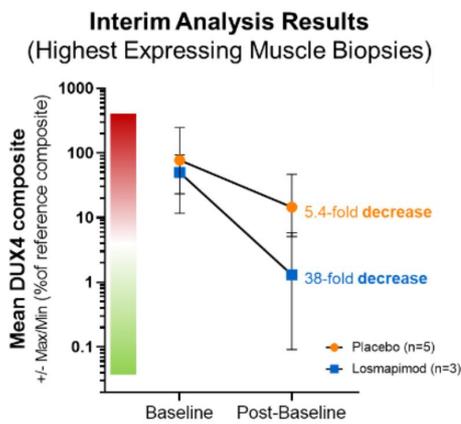
The original design of ReDUX4 included a muscle biopsy at week 16 during the 24-week treatment period followed by an open label extension. Sixteen of the 80 subjects in trial have completed the 24-week treatment period and rolled over to the open label extension portion of the trial. As a result of the COVID-19 pandemic, we extended the ReDUX4 treatment period from 24 to 48 weeks through a protocol amendment to ensure the safety of the subjects and to allow for the opportunity for a biopsy at week 16 as originally intended or at week 36. Approximately 64 subjects who did not complete the original 24-week treatment period continued in the 48-week treatment period in the randomized portion of the trial. The extension from 24 to 48 weeks also allows for a longer assessment in a placebo-controlled design of the skeletal muscle MRI secondary endpoint and the various exploratory clinical endpoints, such as reachable workspace, optimized time up and go test for FSHD, muscle function measures and patient reported outcomes. We expect to present full data from the trial in the second quarter of 2021. We believe that the amendment to the trial protocol provides flexibility to address the challenges presented by the COVID-19 pandemic and supports collection of efficacy and safety data to support continued discussions with regulatory agencies regarding potential registration strategies.

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



In August 2020, we announced results from a pre-specified interim analysis of the primary endpoint of the ReDUX4 trial, which is the reduction from baseline of DUX4-driven gene expression in affected skeletal muscle after subjects have been treated with losmapimod or placebo. Secondary and exploratory endpoints were not assessed as part of this analysis. Results from the interim analysis in the first 29 randomized subjects indicate that DUX4-driven gene expression did not show a separation from placebo at 16 weeks. However, in a pre-specified sensitivity analysis, those with the highest pre-treatment DUX4-driven gene expression in their muscle biopsy sample showed a large reduction in DUX4-driven gene expression following treatment with losmapimod compared to placebo. The highest expressing muscle biopsies represent the top quartile of biopsies assessed based on baseline DUX4-driven gene expression.

The interim results included an analysis of the first 29 subjects who completed their 16-week biopsy out of the 80 subjects enrolled. Pharmacokinetics, demographics and the primary endpoint were assessed. The interim analysis was not powered for statistical significance and did not include individual patient level data. Subjects were randomized to receive an oral dose of losmapimod 15mg (n=15) or placebo (n=14) twice per day. While results showed a significant reduction in DUX4-driven gene expression in the muscle biopsies of subjects whose baseline biopsy showed the highest levels of DUX4 gene expression (38-fold decrease with losmapimod, n=3, and 5.4 fold-decrease with placebo, n=5), the population level data analysis of the reduction in DUX4-driven gene expression from all 29 subjects did not show a separation of losmapimod from placebo (3.7 fold increase with losmapimod, n=15, and 2.8 fold increase with placebo, n=14). Results indicated that muscle biopsies within the higher range of DUX4-driven gene expression at baseline may be needed to observe a reduction. These interim results are shown in the graphics below.



Highest expressing muscle biopsies represent the top quartile of biopsies assessed for baseline DUX4-driven gene expression

Clinical Trial: ReDUX4 Open Label Extension

In February 2020 we initiated an open label extension of the ReDUX4 trial to enable patients who have completed the 24-week or 48-week treatment period with losmapimod or placebo in ReDUX4 to receive long term treatment with losmapimod. This open label extension includes clinical assessments of safety and efficacy every three months, whole-body musculoskeletal MRI every six months, and a muscle needle biopsy once after six months of treatment. We anticipate that this trial will continue until such time as the drug is approved and available in the commercial setting or the clinical development of losmapimod in FSHD is terminated.

Clinical Trial: Phase 2 Open Label Study Trial

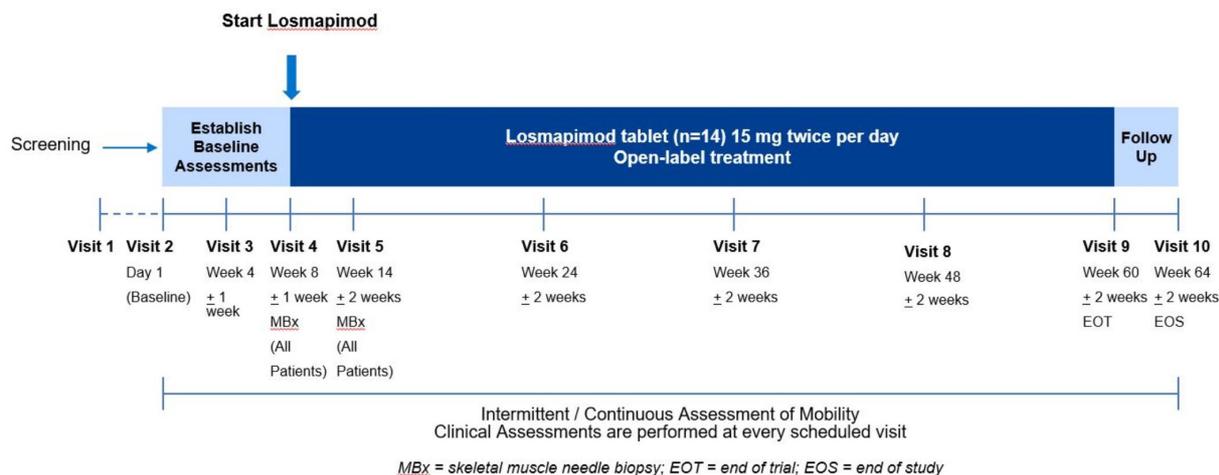
In parallel with the Phase 2b clinical trial, we also initiated in August 2019 an open label, single center Phase 2 clinical trial of losmapimod in up to 16 patients with FSHD1 and clinical severity scores of two to four on the Ricci scale. Patients receive tablets containing 15 mg of losmapimod twice per day for up to 52 weeks. The treatment period is preceded by eight weeks of pre-treatment assessments to establish a baseline for musculoskeletal MRI biomarkers and clinical outcome assessments. We also performed an outpatient mobility assessment using wearable sensors. We are conducting the trial at a single center 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 p38 α / β 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 had a pre-treatment biopsy and we will obtain a second muscle needle biopsy from each patient after four or eight weeks of treatment. The original trial design included an additional biopsy during chronic treatment at week 48, but we have removed this assessment from the trial protocol because the open label extension of ReDUX4 includes a biopsy during chronic 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 are RWS, FSHD-TUG, muscle strength, motor function ability and generic and FSHD-specific patient reports of quality of life and activities of daily living. Other exploratory assessments include the six minute walk test, spirometry, and muscle ultrasound. There is also 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-6058 to elevate the level of fetal hemoglobin for the treatment of patients with certain hemoglobinopathies, namely sickle cell disease and for certain types of β -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 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, vaso-occlusive crises, and inhibition of hemoglobin S polymerization. The four drug treatments approved in the United States are hydroxyurea, voxelotor, crizanlizumab, 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. Voxelotor, marketed by Global Blood Therapeutics, is approved under accelerated approval as a hemoglobin polymerization inhibitor. Crizanlizumab, marketed by Novartis AG, or Novartis, is approved for the reduction in the frequency of vaso-occlusive crises.

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.

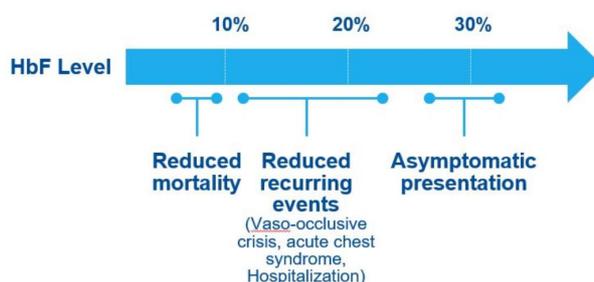
While multiple experimental approaches to treat SCD are being explored in clinical trials, the majority are focused on symptomatic relief or gene therapy approaches. Symptomatic approaches under investigation aim to affect issues associated with cell adhesion, sickling, thrombosis and iron homeostasis. We anticipate that a novel orally available therapy that affects the root cause of SCD may be used in combination with symptomatic therapeutics. Novartis and Global Blood Therapeutics, Inc. have received approval for therapies 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 β -subunits and two hemoglobin α -subunits. In patients with SCD, hemoglobin is composed of two mutant β -subunits and two α -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 α -subunits and two γ -subunits. Shortly after birth, the genes encoding the γ -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 β -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. 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-6058 may address the root cause of SCD through this mechanism of action.

Overview of β -Thalassemia

β -thalassemia is a rare blood disorder associated with the absence or reduced production of β -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 α -globin chains that cause destruction of RBCs. The severity of the phenotype is related to the degree of imbalance between α - and non- α -globin chain synthesis. The absence of β -globin due to *HBB* gene deletions is referred to as β^0 thalassemia. Other *HBB* gene alterations allow some β -globin to be produced but in reduced amounts. A reduced amount of β -globin is called β^+ thalassemia. Many patients with β -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 β -thalassemia per year of whom 25,000 require blood transfusions. Patients with β -thalassemia are primarily treated by hematologists.

β -thalassemia has been clinically characterized into three forms, depending on disease severity: major, intermedia and minor. The most severe form, β -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 β -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. β -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 β -thalassemia minor suffer from very mild anemia and generally do not require treatment. Having either β^0 or β^+ 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 β -thalassemia is frequent blood transfusions to manage anemia. The only potentially curative therapy for β -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 ZYNTEGLO, a gene therapy developed by bluebird bio, Inc., or bluebird, for the treatment of adult and adolescent patients with transfusion-dependent β -thalassemia and with certain genotypes, in Europe in June 2019. bluebird has initiated a rolling biologics license application, or BLA, submission for betibeglogene autotemcel in the United States, which is expected to be completed in mid-2021. Acceleron in collaboration with Celgene Corp., or Celgene, received FDA and EMA approval for luspatercept, an erythroid maturation agent for the treatment of adult patients with anemia associated with β -thalassemia and who require frequent transfusions. There are also multiple other experimental approaches to treat β -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 β -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-6058 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-6058, a novel small molecule inhibitor of the HbF drug target.

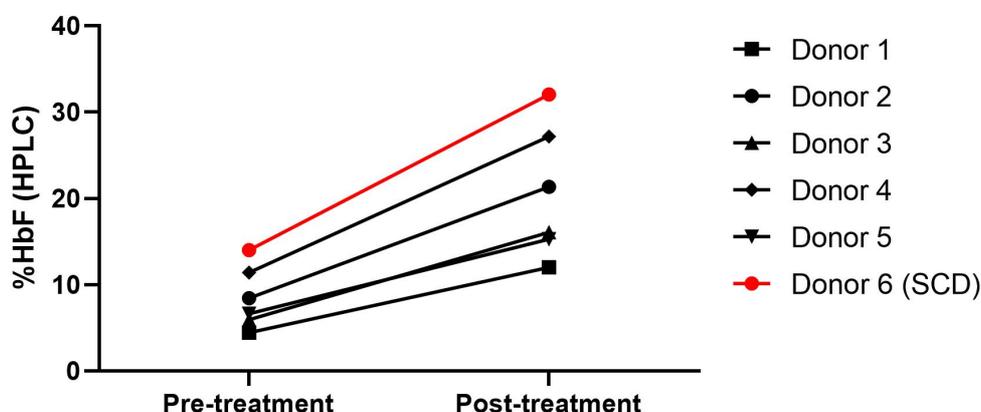
FTX-6058

FTX-6058 is our novel small molecule designed to bind EED and inhibit the transcriptional silencing activity of PRC2. FTX-6058 exhibits fetal hemoglobin induction and 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-6058 in preclinical animal models and observed that its profile supports once daily oral administration. We have not observed any off-target concerns in our *in vitro* profiling studies, and we have completed GLP *in vivo* toxicology studies to evaluate FTX-6058. We initiated our Phase 1 clinical trial of FTX-6058 in healthy adult volunteers in the fourth quarter of 2020. In addition, we anticipate initiating a clinical trial of FTX-6058 in patients with SCD in the second half of 2021.

Preclinical Studies

We have observed *in vitro* and *in vivo* activation of the *HBG1/2* genes in preclinical studies with FTX-6058. We observed that FTX-6058 elevated levels of fetal hemoglobin with minimal adverse effects 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 healthy human donors and one SCD donor after seven days of drug treatment. FTX-6058 showed a significant elevation of fetal hemoglobin over baseline in each of these six donor cell lines. We have conducted additional preclinical profiling in CD34+ derived cells and observed that treatment with FTX-6058 increased HbF levels to approximately 30% of total hemoglobin, as measured by mass spectrometry, high performance liquid chromatography, and fast protein liquid chromatography techniques. The elevation of HbF observed with FTX-6058 was significantly greater than we observed with hydroxyurea in these cell models.

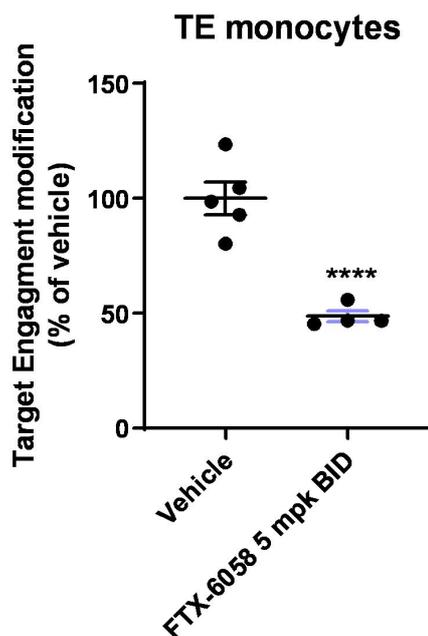
**Effect of FTX-6058 treatment
in differentiated primary human CD34+ cells**



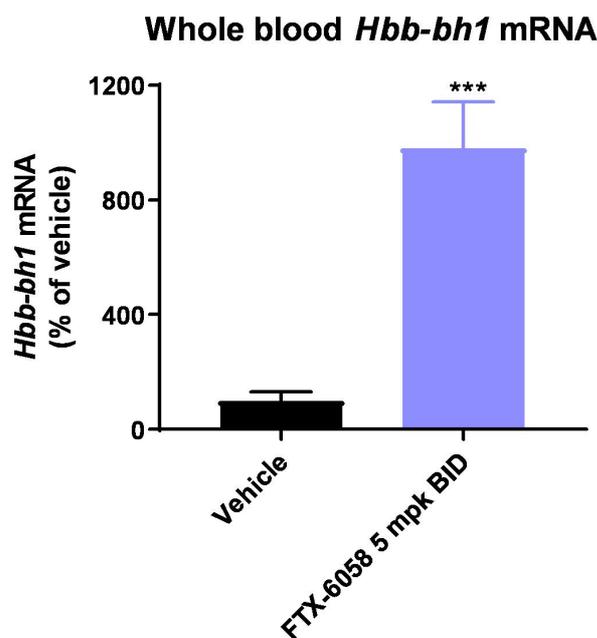
Additionally, we compared the effect of FTX-6058 in CD34+ derived cells relative to that of hydroxyurea. We observed that hydroxyurea had a minimal impact on fetal hemoglobin elevation, whereas we observed that FTX-6058 significantly elevated fetal hemoglobin. In cells treated with the combination of FTX-6058 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 of FTX-6058. FTX-6058 inhibited activity of PRC2, which is responsible for catalyzing tri-methylation of lysine 27 on histone H3 (H3K27me3). As a result, target engagement was assessed by quantifying H3K27me3 levels. 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-6058 engaged the drug target *in vivo* and modulated the endogenous mouse globin gene expression program. The results of this study are depicted below.

Target engagement modification in mouse blood cells

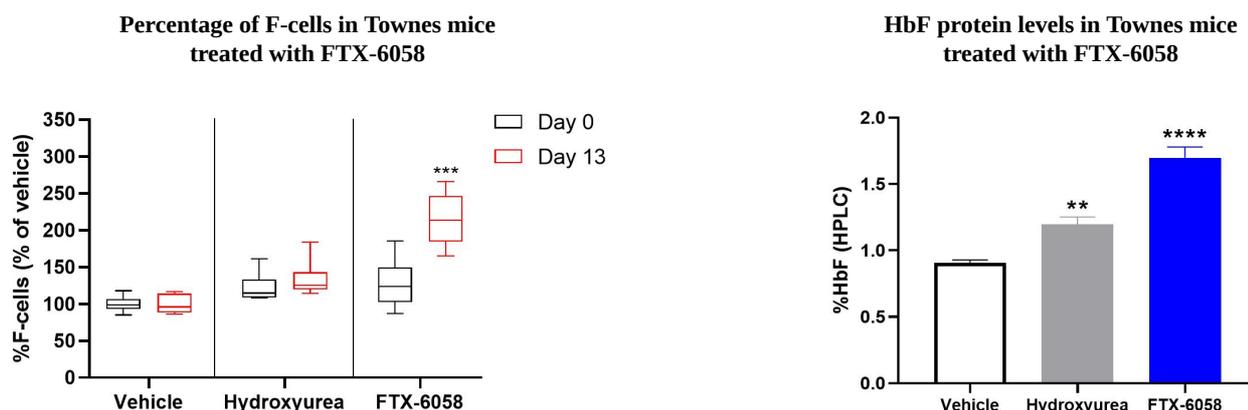


Mouse embryonic globin mRNA levels



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-6058 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-6058 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-6058 resulted in a significant increase in fetal hemoglobin expressing cells, or F-cells, and HbF protein levels after 13 days of dosing at 5 mg/kg once per day whereas hydroxyurea resulted in modest increases in F-cells and HbF.



In the graphic on the left, we quantified the percentage of F-cells as a percentage of total cells (%F-cells) for the three 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 three treatment conditions, quantifying HbF protein as a percentage of total hemoglobin. Each value represents the mean value from eight mice per treatment after 13 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 FTX-6058 was less than 0.001 for both studies and the p-value for hydroxyurea in the study depicted on the right was less than 0.01.

Our Development Plan for FTX-6058

We initiated a Phase 1 clinical trial of FTX-6058 in the fourth quarter of 2020 to evaluate the safety, tolerability and pharmacokinetics of FTX-6058 in healthy adult volunteers.

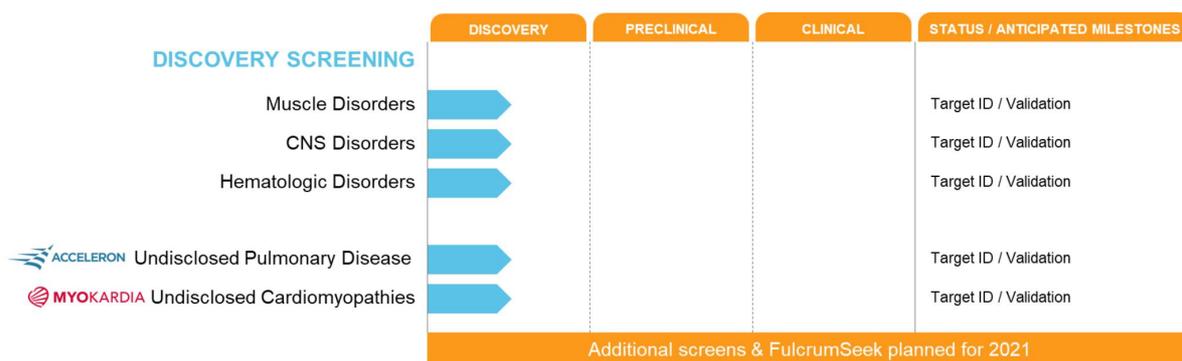
The Phase 1 clinical trial of FTX-6058 in healthy adult volunteers is comprised of four parts. Part A is a randomized, double-blind, placebo-controlled, single ascending dose study in up to six cohorts. Part B is a randomized, double-blind, placebo-controlled, multiple ascending dose study in up to four cohorts dosed once daily for 14 days. Part C is an open label pilot food effect study in subjects randomized to take FTX-6058 with and without a high-fat meal, and Part D is an open label study to evaluate the potential of FTX-6058 to induce a liver enzyme known as CYP3A, which is involved in drug metabolism. We expect to present data from the Phase 1 clinical trial in mid-2021.

In addition, we anticipate initiating a clinical trial of FTX-6058 in patients with SCD in the second half of 2021.

We expect that our target SCD patient population will be SCD patients with inadequate disease control and that concomitant use of hydroxyurea and/or L-glutamine will be allowed when available. We also expect to evaluate FTX-6058 in clinical trials for the treatment of β -thalassemia.

Discovery Screening Programs

We have leveraged our proprietary product engine to discover targets that we are pursuing with small molecules for FSHD, SCD and β -thalassemia. We are leveraging the broad applicability of our product engine to discover drug targets for other rare, genetically defined diseases across neuromuscular, muscular, hematologic and CNS disorders.



Our target identification strategy and approach continue to evolve. In addition to conducting screens to identify targets that modulate the expression of a single root cause gene, we are able to simultaneously interrogate multiple (approximately 10) root cause genes and to monitor effects on cell health all in a single screen (i.e., multiplexed screening). We believe that this new approach provides significant efficiencies in productivity and allows us to test multiple hypotheses in parallel. Importantly, the expansion of FulcrumSeek with the use of high content molecular profiling, including RNAseq and cellular imaging, allows us to simultaneously measure the expression of 8,000-10,000 genes and integrate key measures related to cell health and biology, which enables us to scale our screening capacity and productivity. With the use of our small molecule probe library and our functional genomics capabilities, we aim to conduct target identification at a significantly increased scale and with cost-effectiveness. Moreover, we are using our product engine in hypothesis testing mode and in hypothesis generation mode, which we expect to increase the probability of identifying attractive targets to advance in our portfolio or in collaboration with partners.

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, as amended in September 2020, 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, including a \$2.5 million milestone payment we made to GSK during the year ended December 31, 2019 upon the initiation of a Phase 2 clinical trial, 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.

Collaboration and License Agreement with Acceleron

In December 2019, we entered into a collaboration and license agreement with Acceleron to identify biological targets to modulate specific pathways associated with a targeted indication within the pulmonary disease space. Under the terms of the collaboration and license agreement, we granted Acceleron an exclusive worldwide license under certain intellectual property rights to make, have made, use, sell, have sold, import, export, distribute and have distributed, market, have marketed, promote, have promoted, or otherwise exploit molecules and products directed against or expressing certain biological targets identified by us for the treatment, prophylaxis, or diagnosis of a targeted indication within the pulmonary disease space, or the Indication.

Pursuant to a mutually agreed research plan, we will perform assay screening and related research activities to identify and validate potential biological targets for further research, in order to support the development, manufacture and commercialization of product candidates by Acceleron. Upon completion of the research activities, we will deliver a data package to Acceleron with respect to the biological targets identified by us in the conduct of the research activities for the treatment, prophylaxis, or diagnosis of the Indication. Within a designated period of receipt of the data package, Acceleron will have the right to designate a specified number of the biological targets identified by us for Acceleron's research, development, manufacture and commercialization of products or molecules directed to such targets for the treatment, prophylaxis, or diagnosis of the Indication, or the Targets. If Acceleron does not designate any Targets during the designated period, then the agreement will automatically terminate. If Acceleron designates one or more Targets, then Acceleron will be obligated to use commercially reasonable efforts to seek regulatory approval for one product directed to a Target in certain specified countries. Upon receipt of regulatory approval for any product directed to a Target, Acceleron must use commercially reasonable efforts to commercialize such product in certain specified countries.

While we are performing the research activities pursuant to the research plan and for a specified period thereafter, we may not research, develop, manufacture, commercialize, use, or otherwise exploit any compound or product for the treatment, prophylaxis, or diagnosis of the Indication other than for Acceleron. While we are performing the research activities pursuant to the research plan and for a specified period thereafter, other than for Acceleron, we may not research, develop, manufacture, commercialize, use, or otherwise exploit any compound or product for the treatment, prophylaxis, or diagnosis of the Indication that is directed against certain specified biological targets identified by us in the performance of the research activities.

Acceleron may also request that we perform medicinal chemistry services related to the generation and optimization of molecules directed against or expressing biological targets for the treatment, prophylaxis, or diagnosis of the Indication beyond the scope of the research plan. If we agree to provide such medicinal chemistry services, we and Acceleron will negotiate to determine the scope, timeline and budget for such medicinal chemistry services.

Under the agreement, Acceleron made a \$10.0 million upfront payment to us. We will be entitled to research milestone payments of up to \$18.5 million in the aggregate upon achievement of specified research milestones. Additionally, we will be entitled to development milestone payments of up to \$135.0 million in the aggregate upon the first achievement of specified clinical and regulatory milestones by a product directed to a Target, and up to \$67.5 million in the aggregate upon the second achievement of specified clinical and regulatory milestones by a product directed to a Target. We will also be entitled to sales milestone payments of up to \$145.0 million in the aggregate upon the achievement of one-time aggregate annual worldwide net sales milestones for the first product directed to a Target to achieve such milestones, and up to \$72.5 million in the aggregate upon the achievement of one-time aggregate annual worldwide net sales milestones for the second product directed to a Target to achieve such milestones. To date, we have achieved \$2.0 million of specified research milestones. Acceleron will also pay us tiered royalties ranging from a mid single-digit percentage to a low double-digit percentage based on Acceleron's, and any of its affiliates' and sublicensees', annual worldwide net sales of products directed to any Target. The royalties are payable on a product-by-product basis during a specified royalty term, and may be reduced in specified circumstances.

The agreement continues on a country-by-country and Target-by-Target basis until the last to expire royalty term for a product directed to such Target, at which time the agreement expires with respect to such Target 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. Acceleron also has the right to terminate the agreement for convenience in its entirety or on a Target-by-Target and molecule-by-molecule basis with respect to any molecule directed against a Target.

Collaboration and License Agreement with MyoKardia, a wholly owned subsidiary of Bristol-Myers Squibb Company

In July 2019, we entered into a collaboration and license agreement with MyoKardia, or the MyoKardia Collaboration Agreement, to identify biological targets that are capable of modulating genes of interest with relevance to certain genetically defined cardiomyopathies. Under the terms of the MyoKardia Collaboration Agreement, we granted MyoKardia an exclusive worldwide license under certain intellectual property rights to research, develop, make, have made, use, have used, sell, have sold, offer for sale, have offered for sale, import, have imported, export, have exported, distribute, have distributed, market, have marketed, promote, have promoted, or otherwise exploit products directed against certain biological targets identified by us that are capable of modulating certain genes of interest with relevance to certain genetically defined cardiomyopathies.

Pursuant to a mutually agreed research plan, we will perform assay screening and related research activities to identify and validate up to a specified number of potential cardiomyopathy gene targets, or the Identified Targets, for further research, development, manufacture and commercialization by MyoKardia. We and MyoKardia will work together to determine how best to advance at each stage of the research activities under the research plan and to identify which of the Identified Targets, if any, meet the criteria set forth in the research plan, or the Cardiomyopathy Target Candidates. Upon completion of the research plan, the parties will work together to prepare a final data package and MyoKardia may designate certain Cardiomyopathy Target Candidates for MyoKardia's further exploitation under the MyoKardia Collaboration Agreement, or the Cardiomyopathy Targets. If MyoKardia does not designate any Cardiomyopathy Targets during the designated period, then the MyoKardia Collaboration Agreement will automatically terminate. If MyoKardia designates one or more Cardiomyopathy Targets, then MyoKardia will be obligated to use commercially reasonable efforts to seek regulatory approval for and to commercialize one product directed against an Identified Target in certain specified countries.

During the period in which we are performing the research activities pursuant to the research plan, or the Research Term and for a specified period beyond the Research Term if MyoKardia designates a Cardiomyopathy Target, we may only use the data generated from such research activities for MyoKardia in accordance with the MyoKardia Collaboration Agreement. During the Research Term and for a specified period thereafter, we may not research, develop, manufacture, commercialize, use, or otherwise exploit any compound or product (a) that is a compound or product under the MyoKardia Collaboration Agreement that is directed against the Cardiomyopathy Target Candidates for the treatment, prophylaxis, or diagnosis of any indication or (b) for the treatment of any genetically defined cardiomyopathies shown to be related to certain specified genes of interest that are modulated by the Cardiomyopathy Targets.

Under the MyoKardia Collaboration Agreement, MyoKardia made a \$10.0 million upfront payment and a \$2.5 million payment as prepaid research funding to us in July 2020. MyoKardia will also reimburse us for the costs of the research activities not covered by the prepaid research funding, up to a maximum amount of total research funding (including the prepaid research funding). Upon the achievement of specified preclinical, development and sales milestones, we will be entitled to preclinical milestone payments, development milestone payments and sales milestone payments of up to \$298.5

million in the aggregate per target for certain Identified Targets, and of up to \$150.0 million in the aggregate per target for certain other Identified Targets. MyoKardia will also pay us tiered royalties ranging from a mid single-digit percentage to a low double-digit percentage based on MyoKardia's, and any of its affiliates' and sublicensees', annual worldwide net sales of products under the MyoKardia Collaboration Agreement directed against any Identified Target. The royalties are payable on a product-by-product basis during a specified royalty term, and may be reduced in specified circumstances.

The MyoKardia Collaboration Agreement continues on a country-by-country and product-by-product basis until the last to expire royalty term for a product, at which time the MyoKardia Collaboration Agreement expires with respect to such product in such country. Either party has the right to terminate the MyoKardia Collaboration Agreement if the other party has materially breached in the performance of its obligations under the MyoKardia Collaboration Agreement and such breach has not been cured within the applicable cure period. MyoKardia also has the right to terminate the MyoKardia Collaboration Agreement for convenience in its entirety or on a target-by-target, product-by-product or molecule-by-molecule basis.

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 February 25, 2021, we owned or in-licensed eight U.S. patents, three U.S. pending non-provisional patent applications and related pending foreign patent applications, two pending Patent Cooperation Treaty, or PCT, applications and two U.S. provisional patent applications.

The intellectual property portfolio for our most advanced programs as of February 25, 2021, 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 patents, 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 February 25, 2021, we owned two U.S. patents, two U.S. pending non-provisional patent applications and related foreign patent applications, and one U.S. pending provisional application that relate to our p38 α/β program, relating to methods of using losmapimod and certain other p38 inhibitors for the treatment of FSHD. These patents and patent applications are expected to expire in 2038.

Losmapimod is also 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 of February 25, 2021, we control through our exclusive licensing agreement with GSK six issued U.S. patents and related foreign patents and patent applications, all relating to losmapimod and its pharmaceutical compositions. The U.S. patents and related foreign patents directed to losmapimod composition of matter are expected to expire in 2023.

FTX-6058

As of February 25, 2021, the intellectual property portfolio for our FTX-6058 program include two owned PCT applications and two pending U.S. patent applications directed in part to pharmaceutical compositions as well as to methods for using and making these compositions. In order to continue to pursue protection based on PCT applications, we will need to nationalize the international applications into U.S. non-provisional patent applications and ex-U.S. applications prior to the applicable expiration deadline of the PCT applications. If issued, any patents that may issue from the U.S. non-provisional patent applications and/or foreign patent applications would be projected to have statutory expiration dates between 2039 and 2040, excluding any additional term for patent term adjustments or patent term extension, if applicable.

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 have obtained sufficient losmapimod tablets, or drug product, from GSK to complete our ongoing Phase 2 clinical trials in FSHD. We believe that we have received a sufficient quantity of losmapimod API from GSK to complete further clinical trials in FSHD. We have engaged a contract manufacturing organization to prepare our own API and to manufacture losmapimod tablets. We believe that we have all the necessary information from GSK to enable the required technology transfers to contract manufacturing organizations.

We have obtained sufficient quantities of FTX-6058 to complete our ongoing Phase 1 clinical trial from a contract manufacturing organization.

We expect to continue to rely on third parties for the manufacture of FTX-6058 for any future clinical trials and for the manufacture of 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 or emergency use authorizations 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.

SCD

Approved drug treatments for SCD focus primarily on the management and reduction of pain episodes, vaso-occlusive crises, and inhibition of hemoglobin S polymerization. The four drug treatments approved in the United States are hydroxyurea, voxelotor, crizanlizumab, 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. Voxelotor, marketed by Global Blood Therapeutics, is approved under accelerated approval as a hemoglobin polymerization inhibitor. Crizanlizumab, marketed by Novartis, is approved for the reduction in the frequency of vasoocclusive crises. 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-6058 could face competition from a number of different therapeutic approaches in development for patients with SCD. EpiDestiny, Inc., or EpiDestiny, in collaboration with Novo Nordisk A/S, is evaluating EPI01, a small molecule designed to increase production of fetal hemoglobin, which has completed a Phase 1 clinical trial. Imara, Inc. is evaluating IMR-687, a PDE9 inhibitor, in Phase 2a and Phase 2b clinical trials in patients with sickle cell anemia. Agios Pharmaceuticals, Inc., is evaluating mitapivat, a PKR activator, in a Phase 1 clinical trial in patients with SCD. Forma Therapeutics Holdings, Inc., is evaluating FT-4202, a PKR activator, in a Phase 2/3 clinical trial. Takeda Pharmaceutical Company Limited, is evaluating TAK-755, recombinant ADAMTS13 protein, in a Phase 1/2 clinical trial in participants with baseline health SCD and SCD with acute vaso-occlusive crisis. Pfizer, is evaluating PF-07059013, a hemoglobin subunit beta modulator, in a Phase 1 clinical trial. CRISPR Therapeutics AG (in collaboration with Vertex Pharmaceuticals Incorporated, or Vertex), is evaluating CTX001, a gene therapy, in a Phase 1/2 clinical trial. Aruvant Sciences, Inc. is evaluating ARU-1801, a gene therapy, in a Phase 1/2 clinical trial. CSL Behring, is evaluating CSL200 CAL-H, a gene therapy, in a Phase 1 clinical 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, in a Phase 1/2 clinical trial. There are also several other gene editing approaches being evaluated by Intellia Therapeutics, Inc. (in collaboration with Novartis) and Editas Medicine, Inc. Pfizer conducted a Phase 1b clinical trial with PF-04447943, a PDE9 inhibitor, in patients with SCD.

β-thalassemia

The current standard of care for many patients with β-thalassemia is frequent blood transfusions to manage anemia. The one drug treatment approved in the United States is luspatercept. Luspatercept, marketed by Celgene, is approved as an erythroid maturation agent for the treatment of adult patients with anemia associated with β-thalassemia and who require regular red blood cell transfusions. The only potentially curative therapy for β-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 β-thalassemia and with certain genotypes, in Europe in June 2019. bluebird has initiated a rolling biologics license application, or BLA, submission for betibeglogene autotemcel in the United States, which is expected to be completed in mid-2021. Acceleron in collaboration with Celgene Corp., or Celgene, received FDA and EMA approval for luspatercept, an erythroid maturation agent for the treatment of adult patients with anemia associated with β-thalassemia and who require frequent transfusions.

FTX-6058 could face competition from a number of different therapeutic approaches in development for patients with transfusion-dependent β-thalassemia.

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. Imara, Inc. is evaluating IMR-687, a PDE9 inhibitor, in a Phase 2b clinical trial in patients with β-thalassemia. Agios Pharmaceuticals, Inc., intends to evaluate mitapivat, a PKR activator, in two Phase 3 clinical trials planned for 2021 in patients with non-transfusion dependent and transfusion-dependent β-thalassemia. Forma Therapeutics Holdings, Inc., intends to evaluate FT-4202, a PKR activator, in a Phase 2 clinical trial planned for 2021 in non-transfusion and transfusion-dependent β-thalassemia. Ionis Pharmaceuticals, Inc., is evaluating IONIS TMPRSS6-LRx, an antisense oligonucleotide therapy targeting TMPRSS6, in a Phase 2 clinical trial of non-transfusion dependent β-thalassemia intermedia. Orchard Therapeutics plc is conducting Phase 2 clinical trials of OTL-300, an autologous *ex vivo* gene therapy for the treatment of transfusion-dependent β-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 β-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.

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. 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, 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, including CGP requirements, of the FDA in order to use the study as support for an IND or application for marketing approval. The GCP requirements 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. Similar requirements for posting clinical trial information are present in the European Union (EudraCT) website: <https://eudract.ema.europa.eu/> and other countries, as well.

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.

There is no obligation for a sponsor to make its drug products available for expanded access. If a sponsor has a policy regarding how it responds to expanded access requests, it must make such policy publicly available upon the earlier of initiation of a Phase 2 or Phase 3 clinical trial; or 15 days after the drug or biologic receives designation as a breakthrough therapy, fast track product, or regenerative medicine advanced therapy.

In addition to and separate from expanded access, 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. 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, or PREA, 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. The FDA maintains a list of diseases that are exempt from the requirements of PREA, due to low prevalence of disease in the pediatric population. Under the amended section 505B of the FDA Reauthorization Act of 2017, or FDARA, beginning on August 18, 2020, the submission of a pediatric assessment, waiver or deferral will be required for certain molecularly targeted cancer indications with the submission of an NDA application or supplement to an NDA application. Previously, drugs that had been granted orphan drug designation were exempt from the requirements of the PREA.

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 2021 is \$2,875,842 for an application requiring clinical data. The sponsor of an approved NDA is also subject to an annual program fee, which for fiscal year 2021 is \$336,432. 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. 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 Department of Justice, or 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, known as the reference listed drugs, or RLDs. Abbreviated new drug applications, or ANDAs, generally do not include preclinical and clinical data to demonstrate safety and effectiveness. Instead, the applicant may rely on the preclinical and clinical testing previously conducted for the RLD.

To approve an ANDA, 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 RLD. 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.

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.

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. With regard to patents, the six-month pediatric exclusivity period will not attach to any patents for which a generic (ANDA or 505(b)(2) NDA) applicant submitted a paragraph IV patent certification, unless the NDA sponsor or patent owner first obtains a court determination that the patent is valid and infringed by a proposed generic product.

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. Under Omnibus legislation signed by President Trump on December 27, 2020, the requirement for a subsequent product to show clinical superiority in order to break the previous product's orphan drug exclusivity applies to drugs and biologics that received orphan drug designation before enactment of FDARA in 2017, but have not yet been approved or licensed by FDA.

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 be 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 2030 pursuant to the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act. 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, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These 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.

Since enactment of the ACA, there have been and continue to be, 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. Additionally, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminated the health insurer tax. Further, the Bipartisan Budget Act of 2018, among other things, amended 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". Congress may consider other legislation to replace elements of the ACA during the next Congressional session.

The Trump Administration also took executive actions to undermine or delay implementation of the ACA, including directing 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. On January 28, 2021, however, President Biden rescinded those orders and issued a new Executive Order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care, and consider actions that will protect and strengthen that access. Under this Executive Order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the ACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents.

On November 10, 2020, the Supreme Court heard oral arguments as to whether 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. On February 10, 2021, the Biden Administration withdrew DOJ's support for this lawsuit. A ruling by the Supreme Court is expected sometime this year. 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. To date, there have been several recent U.S. congressional inquiries, as well as proposed and enacted federal and 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. To those ends, President Trump issued five Executive Orders intended to lower the costs of prescription drug products but it is unclear whether, and to what extent, these orders will remain in force under the Biden Administration.

Further, on September 24, 2020, the Trump Administration finalized a rulemaking allowing states or certain other non-federal government entities to submit importation program proposals to FDA for review and approval. Applicants are required to demonstrate that their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. The FDA has issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products).

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 a marketing authorization application, or 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, which is set to replace the current Clinical Trials Directive. The Clinical Trials Regulation will be directly applicable in all EU Member States without the need for any national implementing legislation. It will overhaul the current system of approvals for clinical trials in the EU. The new Clinical Trials Regulation aims to simplify and streamline the approval of clinical trials in the EU. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial will be required to submit a single application for approval of a clinical trial to a reporting EU Member State through an EU Portal. The submission procedure will be the same irrespective of whether the clinical trial is to be conducted in a single EU Member State or in more than one EU Member State.

The Clinical Trials Regulation has not yet become effective. In January 2020, the website of the European Commission reported that the implementation of the Clinical Trials Regulation was dependent on the development of a fully functional clinical trials portal and database, which would be confirmed by an independent audit which was conducted in December 2020, and that the new legislation would come into effect six months after the European Commission publishes a notice of this confirmation. The Clinical Trials Regulation becomes applicable six months after the European Commission publishes notice of this confirmation and has published an expected system “go live” in December 2021. When the Clinical Trials Regulation becomes applicable, the existing Clinical Trial Directive and national legislation put in place to implement the Directive will be repealed. Following implementation of the Clinical Trials Regulation, a transitional period will be in effect for one year where new clinical trial applications can be submitted either under the existing Clinical Trials Directive or under the new 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 with 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 pediatric 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 pediatric 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 2001/83/EC, as amended, and are also subject to EU Member State laws. Direct-to-consumer advertising of prescription medicines is prohibited across the EU.

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.

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. Following protracted negotiations, the United Kingdom left the EU on January 31, 2020. On December 24, 2020, the United Kingdom and the European Union entered into a Trade and Cooperation Agreement, which sets out certain procedures for approval and recognition of medical products in each jurisdiction. 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, as the United Kingdom legislation now has the potential to diverge from European legislation. It remains to be seen how Brexit will impact regulatory requirements for product candidates and products in the United Kingdom in the long-term. The MHRA has recently published detailed guidance for industry and

organizations to follow from January 1, 2021 now that the transition period is over, which will be updated as the United Kingdom's regulatory position on medical products evolves over time.

Furthermore, while the Data Protection Act of 2018 in the United Kingdom that "implements" and complements the EU's GDPR, is now effective in the United Kingdom, it is still unclear whether transfer of data from the European Economic Area, or EEA, to the United Kingdom will remain lawful under GDPR. The Trade and Cooperation Agreement provides for a transitional period during which the United Kingdom will be treated like an EU Member State in relation to processing and transfers of personal data for four months from January 1, 2021. This may be extended by two further months. After such period, the United Kingdom will be a "third country" under the GDPR unless the European Commission adopts an adequacy decision in respect of transfers of personal data to the United Kingdom. The United Kingdom has already determined that it considers all of the EU and EEA member states to be adequate for the purposes of data protection, ensuring that data flows from the United Kingdom to the EU and EEA remain unaffected.

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.

Human Capital and Employees

As of February 25, 2021, we had 73 full-time employees, including a total of 26 employees with M.D. or Ph.D. degrees. Of these full-time employees, 50 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.

We believe that our future success is dependent on attracting, motivating and retaining talented employees. We value the health and wellness of our employees and their families. We aim to create an equitable, inclusive and empowering work environment in which our employees can grow and advance their careers, with the overall goal of developing, expanding and retaining our workforce to support our current pipeline and future business goals. Our success also depends on our ability to attract, engage and retain a diverse group of employees.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and additional employees. Our efforts to recruit and retain a diverse and passionate workforce include providing competitive compensation, including equity compensation, and benefits packages. The principal purposes of our equity incentive plans are to attract, retain and motivate our employees, consultants and directors through the granting of stock-based compensation awards. We offer a comprehensive benefits program that provides resources to help employees manage their health and well-being, finances, and life outside of work, including health insurance and dental care, vision insurance, disability insurance, paid sick leave, a 401(k) plan, and paid vacation time.

Corporate Information

Our principal executive office is located at 26 Landsdowne Street, Cambridge, MA 02139, and our telephone number is 617-651-8851. Our internet website address is www.fulcrumtx.com. The information contained on, or that can be accessed through, our website is not a part of this Annual Report on Form 10-K.

Item 1A. Risk Factors.

Our future operating results could differ materially from the results described in this Annual Report on Form 10-K due to the risks and uncertainties described below. You should consider carefully the following information about risks below in evaluating our business. If any of the following risks actually occur, our business, financial conditions, results of operations and future growth prospects would likely be materially and adversely affected. In these circumstances, the market price of our common stock would likely decline. In addition, we cannot assure investors that our assumptions and expectations will prove to be correct. Important factors could cause our actual results to differ materially from those indicated or implied by forward-looking statements. See page i of this Annual Report on Form 10-K for a discussion of some of the forward-looking statements that are qualified by these risk factors. Factors that could cause or contribute to such differences include those factors discussed below.

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 \$70.8 million for the year ended December 31, 2020 and \$82.7 million for the year ended December 31, 2019. As of December 31, 2020, we had an accumulated deficit of \$221.6 million. To date, we have funded our operations primarily from the sale of shares of our common stock in public offerings, a private placement, and in “at-the-market” offerings, through issuances of convertible preferred stock, and from upfront payments received under our collaboration and license agreements. 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 2b and Phase 2 open label clinical trials for the treatment of facioscapulohumeral muscular dystrophy, or FSHD;
- continue our clinical development of FTX-6058, including our ongoing Phase 1 clinical trial in healthy adult volunteers and our planned clinical trial of FTX-6058 in patients with SCD;
- continue our ongoing preclinical studies;
- 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 our stockholders to lose all or part of their 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 2b and Phase 2 open label clinical trials of losmapimod for the treatment of FSHD, continue our recently initiated Phase 1 clinical trial of FTX-6058 in healthy adult volunteers, prepare for our planned clinical trial of FTX-6058 in patients with SCD, 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, we will 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 2b and Phase 2 open label clinical trials of losmapimod for the treatment of FSHD, our ongoing Phase 1 clinical trial of FTX-6058 in healthy adult volunteers and our planned clinical trial of FTX-6058 for the treatment of SCD;
- the scope, progress, costs and results of discovery research, preclinical development, laboratory testing and clinical trials for our current product candidates in additional indications or for any future product candidates that we may pursue;
- the impact of the COVID-19 pandemic on our business and operations;
- 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;
- the success of our collaborations with Acceleron and MyoKardia;
- our ability to establish and maintain additional strategic collaborations, licensing or other arrangements and the financial terms of such arrangements;
- the payment or receipt of milestones, royalties and 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 December 31, 2020, we had cash, cash equivalents, and marketable securities of approximately \$112.9 million. We believe that our cash, cash equivalents, and marketable securities as of December 31, 2020, together with the net proceeds from the sale of our shares of common stock in a public offering on January 22, 2021 of \$46.4 million, will enable us to fund our operating expenses and capital expenditure requirements into the fourth quarter of 2022. 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, 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, our stockholders' ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights as common stockholders. 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 stockholders 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, establishing our intellectual property, building our discovery platform, identifying drug targets and potential product candidates, in-licensing assets, producing drug substance and drug product material for use in clinical trials and conducting preclinical studies and conducting clinical trials. 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 stockholders 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, stockholders should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

The ongoing COVID-19 pandemic has and may continue to affect our ability to initiate and complete current or future preclinical studies or clinical trials, disrupt regulatory activities or have other adverse effects on our business and operations. In addition, this pandemic may continue to adversely impact economies worldwide, which could result in adverse effects on our business and operations.

The ongoing COVID-19 pandemic has caused many governments to implement measures to slow the spread of the outbreak through quarantines, travel restrictions, heightened border scrutiny, and other measures. The outbreak and government measures taken in response have also had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred; supply chains have been disrupted; facilities and production have been suspended; and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen. The future progression of the outbreak and its effects on our business and operations are uncertain.

We and our contract manufacturing organizations, or CMOs, and contract research organizations, or CROs, may face disruptions that may affect our ability to initiate and complete preclinical studies or clinical trials, including disruptions in procuring items that are essential for our research and development activities, including, for example, raw materials and API used in the manufacturing of our product candidates, and laboratory supplies for our current and future preclinical studies and clinical trials, in each case, for which there may be shortages because of ongoing efforts to address the outbreak. We and our CMOs and CROs, may face disruptions related to our planned and ongoing clinical trials or future clinical trials arising from delays in IND-enabling studies, manufacturing disruptions, and the ability to obtain necessary institutional review board or other necessary site approvals, as well as enrollment and other delays at clinical trial sites. For example, in the wake of COVID-19, the clinical trial sites for our Phase 2b clinical trial temporarily postponed trial-related activities, impacting our clinical trial execution plans. We may also face difficulties recruiting or retaining patients for our planned and ongoing clinical trials if patients are affected by the virus or are fearful of visiting or traveling to clinical trial sites because of the outbreak. The response to the COVID-19 pandemic may redirect resources with respect to regulatory and intellectual property matters in a way that would adversely impact our ability to progress regulatory approvals and protect our intellectual property. In addition, we may face impediments to regulatory meetings and approvals due to measures intended to limit in-person interactions.

Additionally, the impact of the COVID-19 outbreak in Massachusetts resulted in a temporary reduction in workforce presence at our Cambridge research facility. While we increased workforce presence at our facilities starting in the second quarter of 2020, not all employees have returned to our facility and we cannot be certain that we will not be required to close our facilities in the future as a result of the COVID-19 outbreak. A closure of our facility may substantially impact our discovery and translational activities and may delay the experimentation needed to identify novel drug targets, prosecute such targets, identify development candidates for such targets and identify biomarkers that inform the potential clinical development paths for such targets. Moreover, discovery and implementation of clinical biomarker assays for ongoing clinical trials may be delayed. Furthermore, any negative impact that the outbreak has on the ability of our CROs to deliver data sets and execute on experimentation could cause substantial delays for our discovery activities and materially impact our ability to fuel our pipeline with new product candidates.

The pandemic has already caused significant disruptions in the financial markets, and may continue to cause such disruptions, which could impact our ability to raise additional funds through public offerings and may also impact the volatility of our stock price and trading in our stock. Moreover, it is possible the pandemic will significantly impact economies worldwide, which could result in adverse effects on our business and operations. We cannot be certain what the overall impact of the COVID-19 pandemic will be on our business and it has the potential to adversely affect our business, financial condition, results of operations and prospects.

Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition.

Recent changes in tax law may adversely affect our business or financial condition. On December 22, 2017, the U.S. government enacted the Tax Cuts and Jobs Act, or the TCJA, which significantly reformed the U.S. Internal Revenue Code of 1986, as amended, or the Code. The TCJA, among other things, contained significant changes to corporate taxation, including a reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, the limitation of the tax deduction for net interest expense to 30% of adjusted taxable income (except for certain small businesses), the limitation of the deduction for net operating losses arising in taxable years beginning after December 31, 2017 to 80% of current year taxable income and elimination of net operating loss carrybacks for losses arising in taxable years ending after December 31, 2017 (though any such net operating losses may be carried forward indefinitely), the imposition of a one-time taxation of

offshore earnings at reduced rates regardless of whether they are repatriated, the elimination of U.S. tax on foreign earnings (subject to certain important exceptions), the allowance of immediate deductions for certain new investments instead of deductions for depreciation expense over time, and the modification or repeal of many business deductions and credits.

As part of Congress' response to the COVID-19 pandemic, the Families First Coronavirus Response Act, or FFCR Act, was enacted on March 18, 2020, the CARES Act was enacted on March 27, 2020 and COVID-19 relief provisions were included in the Consolidated Appropriations Act, 2021, or CAA, which was enacted on December 27, 2020. All contain numerous tax provisions. In particular, the CARES Act retroactively and temporarily (for taxable years beginning before January 1, 2021) suspends application of the 80%-of-income limitation on the use of net operating losses, which was enacted as part of the TCJA. It also provides that net operating losses arising in any taxable year beginning after December 31, 2017, and before January 1, 2021 are generally eligible to be carried back up to five years. The CARES Act also temporarily (for taxable years beginning in 2019 or 2020) relaxes the limitation of the tax deductibility for net interest expense by increasing the limitation from 30% to 50% of adjusted taxable income.

Regulatory guidance under the TCJA, the FFCR Act, the CARES Act and the CAA is and continues to be forthcoming, and such guidance could ultimately increase or lessen impact of these laws on our business and financial condition. It is also possible that Congress will enact additional legislation in connection with the COVID-19 pandemic, some of which could have an impact on our company. In addition, it is uncertain if and to what extent various states will conform to the TCJA, the FFCR Act, the CARES Act and the CAA.

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

As of December 31, 2020, we had federal and state net operating loss carryforwards of \$170.7 million and \$170.2 million, respectively, which begin to expire in 2035. Approximately \$139.7 million of the federal net operating losses can be carried forward indefinitely. As of December 31, 2020, we also had federal orphan drug credits of \$3.0 million, which begin to expire in 2040. As of December 31, 2020, we also had federal and state research and development tax credit carryforwards of \$4.6 million and \$2.8 million, respectively, which begin to expire in 2035 and 2030, respectively. 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 net operating losses 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," which is generally defined as a greater than 50% change, by value, in its equity ownership by certain stockholders over a three-year period, is subject to limitations on its ability to utilize its pre-change net operating losses 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 (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 net operating losses and research and development tax credit carryforwards to offset such taxable income may be subject to limitations. Our net operating losses or credits may also be impaired under state law.

There is also a risk that due to regulatory changes, such as suspensions on the use of net operating losses, or other unforeseen reasons, our existing net operating losses could expire or otherwise become unavailable to offset future income tax liabilities. As described above in "Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition," the TCJA, as amended by the CARES Act, includes changes to U.S. federal tax rates and the rules governing net operating loss carryforwards that may significantly impact our ability to utilize our net operating losses to offset taxable income in the future. In addition, state net operating losses generated in one state cannot be used to offset income generated in another state. For these reasons we may be unable to use a material portion of our net operating losses and other tax attributes.

Risks Related to the Discovery and Development of our Product Candidates

We are early in our development efforts, and we only have two product candidates in clinical trials. 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 two product candidates into clinical trials, losmapimod for the treatment of FSHD, and FTX-6058 in healthy adult volunteers. 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;
- allowance by the FDA or other regulatory agencies of the investigational new drug applications, or INDs, clinical trial applications, or CTAs, or other regulatory filings for losmapimod, FTX-6058 and future product candidates;
- expanding and maintaining a workforce of experienced scientists and others to continue to develop our product candidates;
- 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 stockholders any assurance that we will be able to successfully identify additional product candidates with our product engine, including as a result of our collaborations with Acceleron and MyoKardia, advance any 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 two product candidates in clinical development. 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 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.

We have entered into a right of reference and license agreement, or the GSK Agreement, as amended, 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 3,600 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;
- unforeseen global instability, including political instability or instability from an outbreak of pandemic or contagious disease, such as the COVID-19 pandemic, in or around the countries in which we conduct our clinical trials, could delay the commencement or rate of completion of our clinical 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.

For example, in the wake of COVID-19, the clinical trial sites for our Phase 2b clinical trial temporarily postponed trial-related activities, impacting our clinical trial execution plans, and we cannot be certain that we will not face other postponements or similar difficulties in the future.

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, muscular, hematologic and central nervous system disorders. 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 Phase 2b and Phase 2 open label clinical trials of losmapimod in patients with FSHD in Europe and Canada 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 Phase 2b and Phase 2 open label clinical trials of losmapimod in patients with FSHD in Europe and Canada. We may also 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 with respect to losmapimod for the treatment of FSHD. 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. bluebird bio, Inc., Aruvant Sciences, Inc., EpiDestiny, Inc., or EpiDestiny (in collaboration with Novo Nordisk A/S), Imara, Inc., Agios Pharmaceuticals, Inc., Forma Therapeutics Holdings, Inc., Takeda Pharmaceutical Company Limited, Pfizer, Inc., CSL Behring, Intellia Therapeutics, Inc., Editas Medicine, Inc., Sangamo Therapeutics Inc., or Sangamo (in collaboration with Bioverativ Inc.) and CRISPR Therapeutics AG (in collaboration with Vertex Pharmaceuticals, Inc.) are developing therapeutic approaches for patients with sickle cell disease, or SCD. Acceleron (in collaboration with Celgene Corp.), Bellicum Pharmaceuticals, Inc., Kiadis Pharma, Imara Inc., Agios Pharmaceuticals, Inc., Forma Therapeutics Holdings, Inc., Ionis Pharmaceuticals, Inc., 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 β -thalassemia.

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 certain of 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 primarily focus our research and product development on treatments for rare diseases. Given the small number of patients who have the rare 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 for many of the indications that we are evaluating are very small, we may never achieve profitability despite obtaining such significant market share.

The target patient populations for some of the indications we are evaluating 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 rely, and expect to continue 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 manufacture clinical supplies of our product candidates and we expect to rely on third parties to manufacture 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, as well as public health issues (for example, an outbreak of a

contagious disease such as COVID-19), 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 2b and Phase 2 open label clinical trials of losmapimod and our ongoing Phase 1 clinical trial of FTX-6058. We plan to rely on third-party clinical research organizations or third-party research collaboratives to conduct any future clinical trials, including our planned clinical trial of FTX-6058 in patients with SCD. 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, 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 rely, and expect to continue 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 contract with, and plan to continue 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 ongoing 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 have also engaged CMOs to

prepare our own API and to manufacture losmapimod tablets. While we believe that we have all the necessary information from GSK to enable any required technology transfer to a CMO, there can be no assurances that we will be able to effect such transfer in a timely manner.

In addition, although we believe we have obtained sufficient quantities of FTX-6058 from a CMO for the completion of our ongoing Phase 1 clinical trial, we cannot be sure we have correctly estimated our drug product requirements, which could delay, prevent or impair our development efforts.

We expect to rely on third parties for the manufacture of FTX-6058 for any future clinical trials and for the manufacture of any future product candidates for preclinical and clinical testing. 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. 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 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 have entered into, and may in the future enter into, collaborations with third parties for the discovery, 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.

In December 2019, we entered into a collaboration and license agreement with Acceleron to identify biological targets to modulate specific pathways associated with a targeted indication within the pulmonary disease space. In July 2020, we entered into a collaboration and license agreement with MyoKardia to identify and validate potential biological targets for the potential treatment of certain genetically defined cardiomyopathies. 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 other existing or future product candidates. Our likely collaborators for any such sales, marketing, distribution, development, licensing or broader collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. If we 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, including our collaborations with Acceleron and MyoKardia, 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 herein 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. For example, in November 2020, subsequent to our entering into the MyoKardia Collaboration Agreement, MyoKardia was acquired by Bristol-Myers Squibb Company. Bristol-Myers Squibb Company could determine to reprioritize MyoKardia's development programs such that it ceases to diligently pursue the development of our programs and/or cause the agreement between MyoKardia and us to terminate. 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. For example, in December 2019, we entered into a collaboration and license agreement with Acceleron to identify biological targets to modulate specific pathways associated with a targeted indication within the pulmonary disease space, and in July 2020, we entered into a collaboration and license agreement with MyoKardia to identify and validate potential biological targets for the potential treatment of certain genetically defined cardiomyopathies. 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 may also be restricted under existing or future license agreements from entering into agreements on certain terms with potential collaborators. For example, we are restricted by GSK's right of first negotiation under our current license agreement with them. We are also restricted under our collaboration with Acceleron from, directly or indirectly, researching, developing, manufacturing, commercializing, using or otherwise exploiting any compound or product for the treatment, prophylaxis, or diagnosis of a targeted indication within the pulmonary disease space, other than for Acceleron, while we are performing the research activities pursuant to the research plan and for a specified period thereafter. Additionally, we are restricted under our collaboration with Acceleron from researching, developing, manufacturing, commercializing, using, or otherwise exploiting any compound or product for the treatment, prophylaxis, or diagnosis of a targeted indication within the pulmonary disease space that is directed against certain specified biological targets identified by us in the performance of the research activities while we are performing the research activities pursuant to the research plan and for a specified period thereafter. Under our collaboration with MyoKardia, we are restricted from researching, developing, manufacturing, commercializing, using, or otherwise exploiting any compound or product (a) that is a compound or product under the agreement that is directed against certain targets identified by us in the performance of the research activities for the treatment, prophylaxis, or diagnosis of any indication or (b) for the treatment of any genetically defined cardiomyopathies shown to be related to certain specified genes of interest that are modulated by the targets chosen by MyoKardia under our

collaboration, in each case, while we are performing the research activities pursuant to the research plan and for a specified period thereafter.

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-6058 is in early stages and comprises two U.S. non-provisional applications and two PCT applications. We have no issued patents related to FTX-6058 or our SCD or β -thalassemia programs. In order to continue to pursue protection based on the PCT applications, we will need to nationalize these applications into corresponding foreign applications prior to the expiration deadline of the PCT applications. 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. We own one patent covering the use of losmapimod for the treatment of patients with FSHD and we own one patent covering the use of other clinical-stage p38 inhibitors for the treatment of patients with FSHD. In addition, our owned patents and patent applications pertaining to losmapimod are not to the composition but, rather, are directed to certain methods of treating FSHD. We cannot be certain that our pending patent applications related to the losmapimod program will be granted. 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. For example, while we believe that the specific and generic claims contained in our U.S. patent provide protection for the method of using losmapimod for the treatment of FSHD and while we also believe that the specific and generic claims contained in our pending U.S. non-provisional applications provide protection for the pharmaceutical compositions and methods of use for FTX-6058, 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.

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. 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 new uses not covered by our other patents and patent applications. 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, CROs, CMOs, 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, including manufacturing information, to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. 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.

Disruptions at the FDA and other agencies may prolong the time necessary for regulatory submissions to be reviewed and/or new drugs to be approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical employees and stop critical activities. If a prolonged government shutdown were to occur, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. The Trump Administration also took several executive actions that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities.

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.

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. The FDA and EMA have granted orphan drug designation to losmapimod for the treatment of FSHD. We may seek orphan drug designation for our other current and future product candidates.

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. Moreover, if we pursue and obtain approval for the same product for another indication for which we are not entitled to or do not have orphan drug exclusivity, our period of orphan exclusivity will not prevent third parties from obtaining approval for a competing drug containing the same active ingredient for use in this other, non-orphan indication. If that were to occur, the protection we derive from orphan exclusivity may be adversely effected.

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. More recently, under Omnibus legislation signed by President Trump on December 27, 2020, the requirement for a subsequent product to show clinical superiority in order to break the previous product's orphan drug exclusivity applies to drugs and biologics that received orphan drug designation before enactment of FDARA in 2017, but have not yet been approved or licensed by FDA. 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.

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 stockholders 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.

Even if the FDA agrees that we may pursue an accelerated approval NDA submission, that does not guarantee that the NDA will receive an accelerated approval, or a complete response letter, nor does submission of an accelerated approval NDA ensure that the product candidate will receive a faster development or regulatory review process.

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 condition, generally provides a meaningful advantage over available therapies, and demonstrates an effect on a surrogate 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 (i.e., an intermediate clinical endpoint). 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 one or more 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.

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, including conditional authorization, 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, we could face heightened risks with respect to seeking marketing approval in the United Kingdom as a result of the recent withdrawal of the United Kingdom from the European Union, commonly referred to as Brexit. Pursuant to the formal withdrawal arrangements agreed between the United Kingdom and the European Union, the United Kingdom withdrew from the European Union, effective December 31, 2020. On December 24, 2020, the United Kingdom and European Union entered into a Trade and Cooperation Agreement, which sets out certain procedures for approval and recognition of medical products in each jurisdiction. Since the regulatory framework for pharmaceutical products in the United Kingdom covering the quality, safety, and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales, and distribution of pharmaceutical products is derived from European Union 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. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, could prevent us from commercializing any 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 any 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.

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 a minimum of \$11,181 and a maximum of \$22,363 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.

Similar actions are either in place or under way in the United States. There are a broad variety of data protection laws that are applicable to our activities, and a wide range of enforcement agencies at both the state and federal levels that can review companies for privacy and data security concerns based on general consumer protection laws. The Federal Trade Commission and state Attorneys General all are aggressive in reviewing privacy and data security protections for consumers. New laws also are being considered at both the state and federal levels. For example, the California Consumer Privacy Act, which went into effect on January 1, 2020, is creating similar risks and obligations as those created by the GDPR, though the California Consumer Privacy Act does exempt certain information collected as part of a clinical trial subject to the Federal Policy for the Protection of Human Subjects (the Common Rule). Many other states are considering similar legislation. A broad range of legislative measures also have been introduced at the federal level. Accordingly, failure to comply with federal and state laws (both those currently in effect and future legislation) regarding privacy and security of personal information could expose us to fines and penalties under such laws. There also is the threat of consumer class actions related to these laws and the overall protection of personal data.

Given the breadth and depth of changes in data protection obligations, preparing for and complying with these 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. If reimbursement of our products is unavailable or limited in scope, our business could be materially harmed.

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.

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, which will stay in effect through 2030 under the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act. The CARES Act suspended the 2% Medicare sequester from May 1, 2020 through December 31, 2020. The American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These 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.

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.

Since the enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the TCJA in 2017, Congress repealed the “individual mandate.” The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. On November 10, 2020, the Supreme Court heard oral arguments as to whether the individual mandate portion of the ACA is an essential and inseverable 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. On February 10, 2021, the Biden Administration withdrew the federal government’s support for overturning the ACA. A ruling by the Supreme Court is expected sometime this year.

The Trump Administration also took executive actions to undermine or delay implementation of the ACA, including directing 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. On January 28, 2021, however, President Biden issued a new Executive Order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care, and consider actions that will protect and strengthen that access. Under this Executive Order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the ACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents. This Executive Order also directs the U.S. Department of Health and Human Services to create a special enrollment period for the Health Insurance Marketplace in response to the COVID-19 pandemic. We cannot predict how federal agencies will respond to such Executive Orders.

Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. To date, there have been several recent U.S. congressional inquiries, as well as 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. To those ends, President Trump issued several executive orders intended to lower the costs of prescription drug products. Certain of these orders are reflected in recently promulgated regulations, including an interim final rule implementing President Trump's most favored nation model, but such final rule is currently subject to a nationwide preliminary injunction. It remains to be seen whether these orders and resulting regulations will remain in force during the Biden Administration. Further, on September 24, 2020, the Trump Administration finalized a rulemaking allowing states or certain other non-federal government entities to submit importation program proposals to the FDA for review and approval. Applicants are required to demonstrate that their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. The FDA has issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products).

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.

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

In countries outside of the United States, 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

Our executive officers, directors and principal stockholders, if they choose to act together, have the ability to control or significantly influence all matters submitted to stockholders for approval.

As of February 25, 2021, our executive officers and directors and our stockholders who owned more than 5% of our outstanding common stock in the aggregate beneficially owned shares representing approximately 46.4% of our capital stock. As a result, if these stockholders were to choose to act together, they would be able to control or significantly influence 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 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 stockholders might otherwise receive a premium for their 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.

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.

An active trading market for our common stock may not be sustained.

Our shares of common stock began trading on the Nasdaq Global Market on July 18, 2019. Given the limited trading history of our common stock, there is a risk that an active trading market for our shares may not continue to develop or be sustained. If an active market for our common stock does not continue to develop or is not sustained, it may be difficult for our stockholders to sell their shares 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 relies, in part, on the research and reports that industry or financial analysts publish about us or our business. There can be no assurance that existing analysts will continue to cover us or that new analysts will begin to cover us. There is also no assurance that any covering analyst will provide favorable coverage. Although we have obtained 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 our stockholders.

The trading price of our common stock has been, and is likely to continue to be volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. 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. 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.

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. Persons who were our stockholders prior to our initial public offering, or IPO, continue to hold a substantial number of shares of our common stock. If such persons sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline.

Moreover, holders of a substantial number of shares of our common stock have rights, 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.

In June 2020, we issued and sold 4,029,411 shares of common stock to investors in a private placement. We have filed a registration statement covering the resale of these shares by the purchasers in the private placement and have agreed to keep such registration statement effective until the date the shares covered by the registration statement have been sold or can be resold without restriction under Rule 144 of the Securities Act of 1933, as amended, or the Securities Act.

We currently have on file with the SEC a universal shelf registration statement which allows us to offer and sell registered common stock, preferred stock, debt securities, depositary shares, warrants and/or units from time to time pursuant to one or more offerings up to an aggregate of \$250 million, at prices and terms to be determined at the time of sale.

In addition, we have filed registration statements registering all shares of common stock that we may issue under our equity compensation plans. These shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates.

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 December 31, 2024, 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:

- 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 may choose to take advantage of some or all of the available exemptions. 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 have incurred and will continue to 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 we have incurred, and particularly after we are no longer an EGC, we will continue to 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 are required to furnish a report by our management on our internal control over financial reporting. However, while we remain an EGC or a smaller reporting company with less than \$100 million in revenue, 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 our stockholders' 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 our stockholders' sole source of gain for the foreseeable future.

Our certificate of incorporation 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 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 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.

Item 1B. Unresolved Staff Comments.

Not applicable.

Item 2. Properties.

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.

Item 3. Legal Proceedings.

We are not currently a party to any material legal proceedings.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant’s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market Information

Our common stock trades under the symbol “FULC” on the Nasdaq Global Market and has been publicly traded since July 18, 2019. Prior to this time, there was no public market for our common stock.

Holders of Our Common Stock

As of February 25, 2021, there were approximately 50 holders of record of shares of our common stock. This number does not include stockholders for whom shares are held in “nominee” or “street” name.

Dividends

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings for use in the operation of our business and do not anticipate paying any dividends on our common stock in the foreseeable future. Any future determination to declare dividends will be made at the discretion of our board of directors and will depend on our financial condition, operating results, capital requirements, general business conditions and other factors that our board of directors may deem relevant.

Unregistered Sales of Equity Securities and Use of Proceeds

Recent Sales of Unregistered Securities

Other than as reported in a Current Report on Form 8-K, we did not sell any securities that were not registered under the Securities Act during the year ended December 31, 2020.

Purchase of Equity Securities by the Issuer and Affiliated Purchasers

Period	Issuer Purchases of Equity Securities			
	(a) Total Number of Shares Purchased ⁽¹⁾	(b) Average Price Paid per Share	(c) Total Number of Shares Purchased as Part of Publicly Announced Plans or Programs	(d) Approximate Dollar Value of Shares that May Yet Be Purchased Under the Plans or Programs
October 1, 2020 through October 31, 2020	1,340	\$ 0.07	—	\$ —
November 1, 2020 through November 30, 2020	4,532	0.07	—	—
December 1, 2020 through December 31, 2020	—	—	—	—
Total	5,872	\$ 0.07	—	\$ —

- (1) Represents shares of unvested common stock that were repurchased by us from a former employee upon termination of employment in accordance with the terms of the applicable employee's restricted stock agreement. We repurchased the shares from the former employee at the original purchase price.

Use of Proceeds from Registered Securities

On July 22, 2019, we completed our IPO, pursuant to which we issued and sold 4,500,000 shares of our common stock at a public offering price of \$16.00 per share. The offer and sale of all of the shares of our common stock in our IPO were registered under the Securities Act pursuant to a registration statement on Form S-1 (File No. 333-232260), which was declared effective by the Securities and Exchange Commission, or SEC, on July 17, 2019. Morgan Stanley & Co. LLC, BofA Securities, Inc. and SVB Leerink LLC acted as joint book-running managers for our IPO. The IPO commenced on July 17, 2019 and terminated without the sale of the 675,000 shares registered for potential issuance upon exercise of the underwriters’ option to purchase additional shares in the IPO.

We received aggregate gross proceeds from our IPO of \$72.0 million, or aggregate net proceeds of \$63.9 million after deducting underwriting discounts and commissions and offering expenses payable by us. None of the underwriting discounts and commissions or offering expenses were incurred or paid to directors or officers of ours or their associates or to persons owning 10% or more of our common stock or to any of our affiliates.

We have used approximately \$49.4 million of the net proceeds from the IPO as of December 31, 2020 to fund the clinical development of losmapimod, to advance our pipeline of clinical-stage and preclinical product candidates, and to research and develop additional preclinical product candidates using our platform, and for working capital and other general corporate purposes. We have invested the unused net proceeds from the offering in cash equivalents and marketable securities. There has been no material change in our planned use of the net proceeds from our IPO as described in our final prospectus filed pursuant to Rule 424(b)(4) under the Securities Act with the SEC on July 18, 2019.

Item 6. Selected Financial Data.

We are a smaller reporting company as defined by Rule 12b-2 of the Exchange Act and are not required to provide the information under this item.

Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations.

The following discussion and analysis of our financial condition and results of operations should be read together with our consolidated financial statements and related notes appearing at the end of this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business, 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 Annual Report on Form 10-K, 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 rare diseases in areas of high unmet medical need. 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. In August 2019, we initiated a Phase 2b clinical trial, known as ReDUX4, and a Phase 2 open label clinical trial of losmapimod, our product candidate for FSHD, to evaluate the efficacy and safety of losmapimod in addressing the underlying cause of FSHD. We expect to present full data from ReDUX4 in the second quarter of 2021.

In the fourth quarter of 2020, we initiated a Phase 1 clinical trial of FTX-6058, our product candidate for certain hemoglobinopathies and a novel upregulator of fetal hemoglobin, to evaluate the safety, tolerability and pharmacokinetics of FTX-6058 in healthy volunteers. We expect to present data from the Phase 1 clinical trial in mid-2021. In addition, we anticipate initiating a clinical trial of FTX-6058 in patients with SCD in the second half of 2021.

In June 2020, we received notification from the FDA that we may proceed with initiating a Phase 3, randomized, double-blind, placebo-controlled trial of losmapimod in higher risk hospitalized adults with COVID-19, or the LOSVID trial. We began enrolling patients in the fourth quarter of 2020. In March 2021, we announced the discontinuation of the LOSVID trial following a strategic review.

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 assets, producing drug substance and drug product material for use in clinical trials and conducting preclinical studies and clinical trials. To date, we have funded our operations primarily from the sale of shares of our common stock in public offerings, a private placement, and in “at-the-market” offerings, or the ATM Offering, through issuances of convertible preferred stock, and from upfront payments received under our collaboration and license agreements.

In January 2021, we issued and sold 4,600,000 shares of our common stock in a public offering at a public offering price of \$11.00 per share, which includes 600,000 shares issued upon the exercise in full by the underwriters of their option to purchase additional shares at the public offering price, less underwriting discounts and commissions. The net proceeds of the offering were \$46.4 million, after deducting underwriting discounts and commissions and estimated offering expenses.

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 \$70.8 million and \$82.7 million for the years ended December 31, 2020 and 2019, respectively. As of December 31, 2020, we had an accumulated deficit of \$221.6 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 2b and Phase 2 open label clinical trials for the treatment of FSHD;
- continue our clinical development of FTX-6058, including our ongoing Phase 1 clinical trial in healthy adult volunteers and our planned clinical trial of FTX-6058 in patients with SCD;
- continue our ongoing preclinical studies;
- 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 a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. 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 December 31, 2020, we had \$112.9 million in cash, cash equivalents, and marketable securities. We believe that our existing cash, cash equivalents, and marketable securities, together with the net proceeds from the sale of our shares of common stock in a public offering on January 22, 2021 of \$46.4 million, will enable us to fund our operating expenses and capital expenditure requirements into the fourth quarter of 2022. 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.”

Components of Results of Operations

Revenue

We have not generated any revenue from product sales and do not expect to generate 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.

In December 2019, we entered into a collaboration and license agreement, or the Acceleron Collaboration Agreement, with Acceleron Pharma Inc., or Acceleron, to identify biological targets to modulate specific pathways associated with a targeted indication within the pulmonary disease space. Under the Acceleron Collaboration Agreement, we granted Acceleron an exclusive worldwide license under certain intellectual property rights to make, have made, use, sell, have sold, import, export, distribute and have distributed, market, have marketed, promote, have promoted, or otherwise exploit molecules and products directed against or expressing certain biological targets identified by us for the treatment,

prophylaxis, or diagnosis of a targeted indication within the pulmonary disease space. The primary goal of the collaboration is to identify and validate potential biological targets for further research in order to support the development, manufacture and commercialization of product candidates by Acceleron for the targeted indication by leveraging our proprietary product engine.

Under the terms of the Acceleron Collaboration Agreement, we received a \$10.0 million upfront payment from Acceleron in December 2019. In December 2020, we achieved \$2.0 million of specified research milestones associated with the Acceleron Collaboration Agreement. We are also eligible to receive up to \$436.5 million in the aggregate in milestone payments with respect to certain research, developmental, clinical, regulatory and sales-related milestones, and tiered royalty payments based on Acceleron's (and any of its affiliates' and sublicensees') annual worldwide net sales of products directed to any identified targets.

For the years ended December 31, 2020 and 2019 we recognized \$6.3 million and zero, respectively, of collaboration revenue under the Acceleron Collaboration Agreement. As of December 31, 2020 and December 31, 2019, we recorded \$7.9 million and \$10.0 million, respectively, of deferred revenue associated with the Acceleron Collaboration Agreement, which is classified as either current or net of current portion in our consolidated balance sheets based on the period over which the revenue is expected to be recognized. As of December 31, 2020, we had received \$1.7 million of cost reimbursement payments and no milestone or royalty payments under the Acceleron Collaboration Agreement. As of December 31, 2020, we recorded unbilled accounts receivable of \$0.5 million related to reimbursable research and development costs under the Acceleron Collaboration Agreement for activities performed during the three months ended December 31, 2020. As of December 31, 2020, we recorded accounts receivable of \$2.0 million associated with the achievement of specified research milestones in December 2020.

In the future, we will recognize additional revenue associated with the \$10.0 million upfront payment and the \$2.0 million of specified research milestones achieved in December 2020 as we satisfy our performance obligation, and from reimbursement of costs incurred under the Acceleron Collaboration Agreement. In the future, we may also generate additional revenue from milestones and royalty payments under the Acceleron Collaboration Agreement. We expect that our revenue will fluctuate from quarter-to-quarter and year-to-year based upon our pattern of performance under the Acceleron Collaboration Agreement and as a result of the timing, amount, and achievement of milestones and reimbursement of costs incurred under the Acceleron Collaboration Agreement.

On July 20, 2020, we entered into a collaboration and license agreement, or the MyoKardia Collaboration Agreement, with MyoKardia, Inc., or MyoKardia, pursuant to which we granted to MyoKardia an exclusive worldwide license under certain intellectual property rights to research, develop, make, have made, use, have used, sell, have sold, offer for sale, have offered for sale, import, have imported, export, have exported, distribute, have distributed, market, have marketed, promote, have promoted, or otherwise exploit products directed against certain biological targets identified by us that are capable of modulating up to a certain number of genes of interest with relevance to certain genetically defined cardiomyopathies. MyoKardia was subsequently acquired by Bristol-Myers Squibb Company in November 2020. The primary goal of the collaboration is to identify and validate potential biological targets for further research, in order to support the development, manufacture and commercialization of product candidates by MyoKardia for the potential treatment of certain genetically defined cardiomyopathies.

Under the terms of the MyoKardia Collaboration Agreement, we received a \$10.0 million upfront payment and a \$2.5 million payment as prepaid research funding in July 2020. MyoKardia will also reimburse us for the costs of the research activities not covered by the prepaid research funding, up to a maximum amount of total research funding (including the prepaid research funding). Upon the achievement of specified preclinical, development and sales milestones, we will be entitled to preclinical milestone payments, development milestone payments and sales milestone payments of up to \$298.5 million in the aggregate per target for certain potential cardiomyopathy gene targets, and of up to \$150.0 million in the aggregate per target for certain other potential cardiomyopathy gene targets. MyoKardia will also pay us tiered royalties ranging from a mid single-digit percentage to a low double-digit percentage based on MyoKardia's, and any of its affiliates' and sublicensees', annual worldwide net sales of products under the MyoKardia Collaboration Agreement directed against any identified target. The royalties are payable on a product-by-product basis during a specified royalty term, and may be reduced in specified circumstances.

For the year ended December 31, 2020 we recognized \$2.5 million of collaboration revenue under the MyoKardia Collaboration Agreement. For the year ended December 31, 2019, we did not recognize any collaboration revenue as we had not yet entered into the MyoKardia Collaboration Agreement. As of December 31, 2020, we have recorded \$10.0 million of

deferred revenue associated with the MyoKardia Collaboration Agreement, which is classified as either current or net of current portion in our consolidated balance sheets based on the period over which the revenue is expected to be recognized. We recorded no deferred revenue associated with the MyoKardia Collaboration Agreement as of December 31, 2019 as we had not yet entered into the MyoKardia Collaboration Agreement. As of December 31, 2020, we had received no cost reimbursement payments and no milestone or royalty payments under the MyoKardia Collaboration Agreement, other than the \$2.5 million payment as prepaid research funding in July 2020. As of December 31, 2020, we recorded no accounts receivable related to reimbursable research and development costs under the MyoKardia Collaboration Agreement.

In the future, we will recognize additional revenue associated with the \$10.0 million upfront payment, and from reimbursement of costs incurred under the MyoKardia Collaboration Agreement, including the \$2.5 million prepaid research funding payment. In the future, we may also generate additional revenue from milestones and royalty payments under the MyoKardia Collaboration Agreement. We expect that our revenue will fluctuate from quarter-to-quarter and year-to-year based upon our pattern of performance under the MyoKardia Collaboration Agreement and as a result of the timing, amount, and achievement of milestones and reimbursement of costs incurred under the MyoKardia Collaboration Agreement.

We may also in the future enter into additional 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 the achievement of a clinical milestone payable to GSK upon the initiation of a Phase 2 clinical trial;
- 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. Non-refundable 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, 2020 and 2019. Pre-development candidate expenses, unallocated expenses and internal research and development expenses are classified separately. Losmapimod external expenses include IPR&D expenses. We nominated FTX-6058 as a development candidate in the third quarter of 2019.

(in thousands)	Year Ended December 31,	
	2020	2019
Losmapimod external expenses	\$ 22,954	\$ 40,390
FTX-6058 external expenses	5,538	3,215
Pre-development candidate expenses and unallocated expenses	14,775	14,948
Internal research and development expenses	15,775	12,519
Total research and development expenses	<u>\$ 59,042</u>	<u>\$ 71,072</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, including in light of COVID-19;
- 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 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 for the treatment of FSHD, advancing FTX-6058 for the treatment of certain hemoglobinopathies, 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 marketable securities.

Results of Operations

Comparison of the Years Ended December 31, 2020 and 2019

The following summarizes our results of operations for the years ended December 31, 2020 and 2019, along with the changes in those items in dollars:

(in thousands)	Year Ended December 31,		Change
	2020	2019	\$
Collaboration revenue	\$ 8,823	\$ —	\$ 8,823
Operating expenses:			
Research and development	59,042	71,072	(12,030)
General and administrative	21,392	13,145	8,247
Total operating expenses	80,434	84,217	(3,783)
Loss from operations	(71,611)	(84,217)	12,606
Other income, net	792	1,540	(748)
Net loss	\$ (70,819)	\$ (82,677)	\$ 11,858

Collaboration Revenue

Collaboration revenue was \$8.8 million for the year ended December 31, 2020. We did not record any collaboration revenue during the year ended December 31, 2019, as we had not yet entered into the MyoKardia Collaboration Agreement and we had not satisfied any portion of our performance obligation under the Acceleron Collaboration Agreement. We recognize revenue under each of the Acceleron Collaboration Agreement and MyoKardia Collaboration Agreement based on our pattern of performance related to the respective identified performance obligation, which is the period over which we will perform research services under each of the Acceleron Collaboration Agreement and MyoKardia Collaboration Agreement. For the year ended December 31, 2020, we recognized \$6.3 million of collaboration revenue under the Acceleron Collaboration Agreement and \$2.5 million of collaboration revenue under the MyoKardia Collaboration Agreement.

Research and Development Expenses

Research and development expense decreased by \$12.1 million from \$71.1 million for the year ended December 31, 2019 to \$59.0 million for the year ended December 31, 2020. The decrease in research and development expense was primarily attributable to a \$25.6 million decrease in IPR&D expenses associated with the recognition of the fair value attributable to the right of reference and license agreement with GSK during the year ended December 31, 2019 as well as a \$2.5 million decrease in milestone expense associated with the milestone payment to GSK upon the initiation of a Phase 2 clinical trial of losmapimod during the year ended December 31, 2019, partially offset by increases in research and development expenses primarily as a result of the following:

- \$12.1 million in increased external research and developments costs, including \$5.2 million in increased manufacturing costs to support our ongoing and planned clinical trials and \$4.9 million in increased costs for external clinical activities as we continued to advance our lead programs;
- \$3.7 million in increased personnel-related costs due to increased headcount, including \$1.1 million of increased stock-based compensation expense; and
- \$0.5 million in increased facility-related costs, including depreciation and other utility and maintenance costs.

General and Administrative Expenses

General and administrative expenses increased by \$8.3 million from \$13.1 million for the year ended December 31, 2019 to \$21.4 million for the year ended December 31, 2020. The increase in general and administrative expenses was primarily attributable to the following:

- \$4.1 million in increased consulting and professional fees, including for insurance premiums, legal services, investor relations, market research, recruiting, and accounting;
- \$3.6 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 \$2.0 million of increased stock-based compensation expense; and
- \$0.5 million in increased facility-related costs, including depreciation and other utility and maintenance costs.

Other Income, Net

Other income, net decreased by \$0.7 million from \$1.5 million for the year ended December 31, 2019 to \$0.8 million for the year ended December 31, 2020. Other income, net during the year ended December 31, 2020 was primarily attributable to a decrease in investment income on our cash, cash equivalents, and marketable securities as a result of an overall decreased rate of return.

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. As of December 31, 2020, we have funded our operations primarily with aggregate gross proceeds of \$300.5 million from the sale of shares of our common stock in public offerings, a private placement, the ATM Offering, through issuances of convertible preferred stock, and from upfront payments received under our collaboration and license agreements. As of December 31, 2020, we had cash, cash equivalents, and marketable securities of \$112.9 million.

On July 22, 2019, we completed an IPO of our common stock and issued and sold 4,500,000 shares of common stock at a public offering price of \$16.00 per share, resulting in net proceeds of \$63.9 million after deducting underwriting discounts and commissions and offering expenses. On June 9, 2020, we issued and sold 4,029,411 shares of common stock in a private placement at a price of \$17.00 per share, resulting in net proceeds of \$64.2 million, after deducting offering costs.

In December 2019, we received a \$10.0 million upfront payment upon execution of the Acceleron Collaboration Agreement and, as of December 2020, we recorded accounts receivable of \$2.0 million in specified research milestones under the Acceleron Collaboration Agreement. In July 2020, we received a \$10.0 million upfront payment and a \$2.5 million payment as prepaid research funding under the MyoKardia Collaboration Agreement.

On August 11, 2020, we filed a shelf registration statement on Form S-3 with the SEC, which was declared effective on August 17, 2020, or the Shelf Registration Statement. Under the Shelf Registration Statement, we may offer and sell up to \$250.0 million of a variety of securities including common stock, preferred stock, warrants, depository shares, debt securities or units during the three-year period that commenced upon the Shelf Registration Statement becoming effective. In connection with the filing of the Shelf Registration Statement, we entered into an Equity Distribution Agreement with Piper Sandler & Co., or Piper Sandler, as sales agent, pursuant to which we may offer and sell shares of our common stock with an aggregate offering price of up to \$75.0 million under the ATM Offering. As of December 31, 2020, we have issued and sold 550,000 shares of common stock under the ATM Offering, resulting in net proceeds of \$5.7 million after deducting offering costs.

On January 22, 2021, we completed a public offering of our common stock and issued and sold 4,600,000 shares of common stock at a public offering price of \$11.00 per share, resulting in net proceeds of \$46.4 million after deducting underwriting discounts and commissions and estimated offering expenses.

Cash Flows

The following table provides information regarding our cash flows for the years ended December 31, 2020 and 2019:

(in thousands)	Year Ended December 31,	
	2020	2019
Net cash used in operating activities	\$ (53,655)	\$ (39,483)
Net cash used in investing activities	(57,138)	(944)
Net cash provided by financing activities	71,132	64,343
Net (decrease) increase in cash, cash equivalents, and restricted cash	\$ (39,661)	\$ 23,916

Net Cash Used in Operating Activities

Net cash used in operating activities was \$53.7 million during the year ended December 31, 2020 compared to net cash used in operating activities of \$39.5 million during the year ended December 31, 2019. The increase in net cash used in operating activities of \$14.2 million was primarily due to increased personnel-related costs, increased research and development costs as we continue to advance our lead programs, and increased general and administrative costs associated with operating as a public company.

Net Cash Used in Investing Activities

Net cash used in investing activities was \$57.1 million during the year ended December 31, 2020 compared to net cash used in investing activities of \$0.9 million during the year ended December 31, 2019. The increase in net cash used in investing activities of \$56.2 million was primarily due to net purchases of marketable securities during the year ended December 31, 2020.

Net Cash Provided by Financing Activities

Net cash provided by financing activities was \$71.1 million during the year ended December 31, 2020 compared to net cash provided by financing activities of \$64.3 million during the year ended December 31, 2019. Net cash provided by financing activities during the year ended December 31, 2020 primarily consisted of net proceeds of approximately \$64.2 million from the completion of the private placement of shares of our common stock in June 2020 and net proceeds of \$5.7 million received under our ATM Offering. Net cash provided by financing activities during the year ended December 31, 2019 primarily consisted of net proceeds of approximately \$64.2 million from the completion of our IPO in July 2019.

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, 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 believe that our existing cash, cash equivalents, and marketable securities as of December 31, 2020, together with the net proceeds from the sale of shares of our common stock in a public offering on January 22, 2021 of \$46.4 million, will enable us to fund our operating expenses and capital expenditure requirements into the fourth quarter of 2022. 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 2b and Phase 2 open label clinical trials of losmapimod for the treatment of FSHD, our ongoing Phase 1 clinical trial of FTX-6058 in healthy adult volunteers and our planned clinical trial of FTX-6058 for the treatment of SCD;
- the scope, progress, costs and results of discovery research, preclinical development, laboratory testing and clinical trials for our current product candidates in additional indications or for any future product candidates that we may pursue;
- the impact of the COVID-19 pandemic on our business and operations;
- 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;
- the success of our collaborations with Acceleron and MyoKardia;
- our ability to establish and maintain additional strategic collaborations, licensing or other arrangements and the financial terms of such arrangements;
- the payment or receipt of milestones, royalties and 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 offerings, debt financings, collaboration arrangements, strategic alliances and marketing, distribution or licensing 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, strategic alliances or marketing, distribution or licensing arrangements 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, 2020 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⁾	\$ 19,462	\$ 2,354	\$ 4,921	\$ 5,221	\$ 6,966
Capital lease obligation	18	18	—	—	—
	<u>\$ 19,480</u>	<u>\$ 2,372</u>	<u>\$ 4,921</u>	<u>\$ 5,221</u>	<u>\$ 6,966</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, including a \$2.5 million milestone payment we made to GSK during the year ended December 31, 2019 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 because 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,” and Note 11 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

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 generally accepted accounting principles 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 reporting 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 consolidated financial statements included elsewhere in this Annual Report on Form 10-K for a description of our other significant accounting policies.

Revenue Recognition

Under the Financial Accounting Standards Board Accounting Standards Codification, or ASC, 606, *Revenue from Contracts with Customers*, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. In applying ASC 606, we perform the following five steps:

1) Identify the contract with the customer

A contract with a customer exists when (i) we enter into an enforceable contract with a customer that defines each party's rights regarding the goods or services to be transferred and identifies the related payment terms, (ii) the contract has commercial substance and (iii) we determine that collection of substantially all consideration for goods and services that are transferred is probable based on the customer's intent and ability to pay the promised consideration.

2) Identify the promises and performance obligations in the contract

Performance obligations promised in a contract are identified based on the goods and services that will be transferred to the customer that are both capable of being distinct, whereby the customer can benefit from the good or service either on its own or together with other readily available resources, and are distinct in the context of the contract, whereby the transfer of the good or service is separately identifiable from other promises in the contract. To the extent a contract includes multiple promised goods and services, we must apply judgment to determine whether promised goods and services are capable of being distinct and distinct in the context of the contract. In assessing whether a promised good or service is distinct, we consider factors such as the research, manufacturing and commercialization capabilities of the customer and the availability of the associated expertise in the marketplace. We also consider the intended benefit of the contract in assessing whether a promised good or service is separately identifiable from other promises in the contract. If these criteria are not met, the promised goods and services are accounted for as a combined performance obligation.

3) Determine the transaction price

The transaction price is determined based on the consideration to which we will be entitled in exchange for transferring goods and services to the customer. If the consideration promised in a contract includes a variable amount, we estimate the amount of consideration to which we will be entitled in exchange for transferring the promised goods or services to a customer. We determine the amount of variable consideration by using the expected value method or the most likely amount method. We include the unconstrained amount of estimated variable consideration in the transaction price. The amount included in the transaction price is constrained to the amount for which it is probable that a significant reversal of cumulative revenue recognized will not occur. At the end of each subsequent reporting period, we re-evaluate the estimated variable consideration included in the transaction price and any related constraint, and if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis in the period of adjustment. Changes to the constraint of variable consideration can have a material effect on the amount of revenue recognized in the period.

If an arrangement includes research and development milestone payments, we evaluate whether the milestones are considered probable of being reached and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are based on the occurrence of events not within our control, such as regulatory approvals, are generally not considered probable of being achieved until the underlying events occur or the associated approvals are received.

For arrangements with licenses of intellectual property that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, we recognize royalty revenue and sales-based milestones at the later of (i) when the related sales occur, or (ii) when the performance obligation to which the royalty has been allocated has been satisfied.

In determining the transaction price, we adjust consideration for the effects of the time value of money if the timing of payments provides us with a significant benefit of financing. We assess our revenue generating arrangements in order to determine whether a significant financing component exists.

4) Allocate the transaction price to the performance obligations in the contract

If the contract contains a single performance obligation, the entire transaction price is allocated to the single performance obligation. Contracts that contain multiple performance obligations require an allocation of the transaction price to each performance obligation on a relative standalone selling price basis, except for any variable consideration that meets the criteria to be allocated entirely to a single performance obligation or to a distinct service that forms part of a single performance obligation.

5) Recognize revenue when or as the Company satisfies a performance obligation

We may satisfy performance obligations over time or at a point in time, depending on the nature of the performance obligation. Revenue is recognized over time if the customer simultaneously receives and consumes the benefits provided by the entity's performance, the entity's performance creates or enhances an asset that the customer controls as the asset is created or enhanced, or the entity's performance does not create an asset with an alternative use to the entity and the entity has an enforceable right to payment for performance completed to date. If the entity does not satisfy a performance obligation over time, the related performance obligation is satisfied at a point in time by transferring the control of a promised good or service to a customer.

For revenue that we recognize over time, we assess whether an input or an output method is the appropriate measure of progress associated with the satisfaction of the performance obligation. In determining the appropriate method for measuring progress, we consider the nature of the good or service that we have promised to transfer to the customer. Output methods recognize revenue on the basis of direct measurements of the value to the customer of the goods or services transferred to date relative to the remaining goods or services promised under the contract. Input methods recognize revenue on the basis of the entity's efforts or inputs to the satisfaction of a performance obligation. Estimates inherent to our measurement of progress associated with the satisfaction of performance obligations based on an input method include the total estimated costs to satisfy the associated performance obligation.

See Note 10, "Collaboration and License Agreements", for further information on the application of ASC 606 to the Acceleron Collaboration Agreement and MyoKardia Collaboration Agreement.

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. Given the lack of public market for our common stock prior to the closing of our IPO and a lack of company-specific historical and implied volatility data, we based 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.

Determination of Fair Value of Common Stock and Series B Preferred Stock prior to our IPO

Prior to our IPO, there was no public market for our common stock. As a result, the estimated fair value of our common stock and Series B preferred stock was 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. We were 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. The third-party valuations of our common stock and our Series B preferred stock 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.

The assumptions underlying these valuations represented our best estimates, which involved inherent uncertainties and the application of judgment.

Following the closing of our IPO, we have determined the fair value of our common stock based on the quoted market price of our common stock on the Nasdaq Global Market.

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

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is disclosed in Note 2 to our consolidated financial statements appearing at the end of this Annual Report on Form 10-K.

Emerging Growth Company Status

The Jumpstart Our Business Startups Act of 2012 permits an “emerging growth company” such as us 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 emerging growth company.

Item 7A. 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 and our investments are in short-term marketable securities, such as corporate bonds and commercial paper. As of December 31, 2020, we had cash, cash equivalents, and marketable securities of \$112.9 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 December 31, 2020, 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, 2020 and 2019.

Item 8. Financial Statements and Supplementary Data.

Our consolidated financial statements, together with the independent registered public accounting firm report thereon, are presented beginning on page F-1 of this Annual Report on Form 10-K.

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Operating Officer (our principal executive officer and principal financial officer, respectively), evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2020. The term “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company’s management, including its principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2020, our Chief Executive Officer and Chief Operating Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management’s Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting for the company. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act as a process designed by, or under the supervision of, a company’s principal executive officer and principal financial officer, or persons performing similar functions, and effected by a company’s board of directors, management, and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that:

- pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of a company’s assets;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that a company’s receipts and expenditures are being made only in accordance with authorizations of a company’s management and directors; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of a company’s assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial

statement preparation and presentation. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Under the supervision of and with the participation of our principal executive officer and principal financial officer, our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2020 based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control—Integrated Framework (2013 framework). Based on this assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2020.

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm due to an exemption established by the JOBS Act for “emerging growth companies”.

Changes in Internal Control over Financial Reporting

There was no change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the three months ended December 31, 2020 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Except to the extent provided below, the information required by this Item 10 will be included in our Definitive Proxy Statement to be filed with the Securities and Exchange Commission, or SEC, with respect to our 2021 Annual Meeting of Stockholders and is incorporated herein by reference.

We post our Code of Business Conduct and Ethics, which 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, in the “Corporate Governance” sub-section of the “Investor Relations” section (ir.fulcrumtx.com) of our corporate website at www.fulcrumtx.com. We intend to disclose on our website any amendments to, or waivers from, the Code of Business Conduct and Ethics that are required to be disclosed pursuant to the disclosure requirements of Item 5.05 of Form 8-K.

Item 11. Executive Compensation.

The information required by this Item 11 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2021 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The information required by this Item 12 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2021 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required by this Item 13 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2021 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 14. Principal Accountant Fees and Services.

The information required by this Item 14 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2021 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 15. Exhibits and Financial Statement Schedules.**(1) Consolidated Financial Statements**

The following documents are included on pages F-1 through F-31 attached hereto and are filed as part of this Annual Report on Form 10-K.

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Consolidated Balance Sheets	F-3
Consolidated Statements of Operations and Comprehensive Loss	F-4
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(2) Financial Statement Schedules

All financial statement schedules have been omitted because they are not applicable, not required, or the information required is shown in the consolidated financial statements or the notes thereto.

(3) Exhibits

The exhibits required by Item 601 of Regulation S-K and Item 15(b) of this Annual Report on Form 10-K are listed in the Exhibit Index immediately preceding the signature page of this Annual Report on Form 10-K. The exhibits listed in the Exhibit Index are incorporated by reference herein.

Item 16. Form 10-K Summary

None.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

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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, 2020 and 2019, the related consolidated statements of operations and comprehensive loss, convertible preferred stock and stockholders' equity (deficit) 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, 2020 and 2019, and the results of its operations and its cash flows for the years then ended, in conformity with U.S. generally accepted accounting principles.

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
March 4, 2021

Fulcrum Therapeutics, Inc.
Consolidated Balance Sheets
(In thousands, except share and per share amounts)

	December 31, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	\$ 57,052	\$ 96,713
Marketable securities	55,862	—
Accounts receivable	2,000	—
Unbilled accounts receivable	531	—
Prepaid expenses and other current assets	4,065	3,370
Total current assets	119,510	100,083
Property and equipment, net	8,397	9,205
Restricted cash	1,092	1,092
Other assets	578	59
Total assets	<u>\$ 129,577</u>	<u>\$ 110,439</u>
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	\$ 4,079	\$ 2,186
Accrued expenses and other current liabilities	7,267	5,496
Deferred lease incentive, current portion	469	469
Deferred revenue, current portion	14,910	3,989
Total current liabilities	26,725	12,140
Deferred rent, excluding current portion	1,649	1,559
Deferred lease incentive, excluding current portion	3,051	3,521
Deferred revenue, excluding current portion	2,971	6,011
Other liabilities, excluding current portion	—	55
Total liabilities	34,396	23,286
Commitments and contingencies (Note 12)		
Stockholders' equity:		
Preferred stock, \$0.001 par value; 5,000,000 shares authorized; no shares issued or outstanding	—	—
Common stock, \$0.001 par value; 200,000,000 shares authorized; 28,067,402 and 23,335,514 shares issued as of December 31, 2020 and December 31, 2019, respectively; 27,941,566 and 22,654,444 shares outstanding as of December 31, 2020 and December 31, 2019, respectively	28	23
Treasury stock, at cost; no shares as of December 31, 2020 and December 31, 2019	—	—
Additional paid-in capital	316,775	237,931
Accumulated other comprehensive loss	(2)	—
Accumulated deficit	(221,620)	(150,801)
Total stockholders' equity	95,181	87,153
Total liabilities and stockholders' equity	<u>\$ 129,577</u>	<u>\$ 110,439</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,	
	2020	2019
Collaboration revenue	\$ 8,823	\$ —
Operating expenses:		
Research and development	59,042	71,072
General and administrative	21,392	13,145
Total operating expenses	<u>80,434</u>	<u>84,217</u>
Loss from operations	(71,611)	(84,217)
Other income, net	792	1,540
Net loss	<u>\$ (70,819)</u>	<u>\$ (82,677)</u>
Cumulative convertible preferred stock dividends	—	(7,128)
Net loss attributable to common stockholders	<u>\$ (70,819)</u>	<u>\$ (89,805)</u>
Net loss per share attributable to common stockholders, basic and diluted	<u>\$ (2.79)</u>	<u>\$ (8.13)</u>
Weighted average number of common shares used in net loss per share attributable to common stockholders, basic and diluted	<u>25,354</u>	<u>11,046</u>
Comprehensive loss:		
Net loss	\$ (70,819)	\$ (82,677)
Other comprehensive loss:		
Unrealized loss on marketable securities	(2)	—
Total other comprehensive loss	<u>(2)</u>	<u>—</u>
Comprehensive loss	<u>\$ (70,821)</u>	<u>\$ (82,677)</u>

The accompanying notes are an integral part of these financial statements.

Fulcrum Therapeutics, Inc.

Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)

(In thousands, except share amounts)

	Series A Convertible Preferred Stock		Series B Convertible Preferred Stock		Common Stock		Treasury Stock		Additional Paid-In Capital	Accumulated other comprehensive loss	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount				
Balance at December 31, 2018	60,000,000	\$ 59,909	40,000,000	\$ 79,761	1,587,953	\$ 2	67,024	\$ —	\$ 4,452	\$ —	\$ (68,124)	\$ (63,670)
Issuance of Series B convertible preferred stock in connection with asset acquisition, net of issuance costs	—	—	12,500,000	25,466	—	—	—	—	—	—	—	—
Conversion of convertible preferred stock into common stock	(60,000,000)	(59,909)	(52,500,000)	(105,227)	16,071,418	16	—	—	165,120	—	—	165,136
Initial public offering, net of underwriting discounts, commissions and offering costs	—	—	—	—	4,500,000	5	—	—	63,867	—	—	63,872
Issuance of common stock under employee benefit plans	—	—	—	—	33,782	—	—	—	253	—	—	253
Vesting of restricted stock awards	—	—	—	—	461,291	—	—	—	15	—	—	15
Repurchase of unvested restricted stock awards	—	—	—	—	—	—	61,450	—	—	—	—	—
Retirement of treasury shares	—	—	—	—	—	—	(128,474)	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	—	—	—	—	4,224	—	—	4,224
Net loss	—	—	—	—	—	—	—	—	—	—	(82,677)	(82,677)
Balance at December 31, 2019	—	\$ —	—	\$ —	22,654,444	\$ 23	—	\$ —	\$ 237,931	\$ —	\$ (150,801)	\$ 87,153
Issuance of common stock in connection with private placement, net of issuance costs	—	—	—	—	4,029,411	4	—	—	64,314	—	—	64,318
Issuance of common stock in "at-the-market" offering, net of issuance costs	—	—	—	—	550,000	1	—	—	5,735	—	—	5,736
Issuance of common stock under employee benefit plans	—	—	—	—	182,359	—	—	—	1,430	—	—	1,430
Vesting of restricted stock awards	—	—	—	—	525,352	—	—	—	15	—	—	15
Repurchase of unvested restricted stock awards	—	—	—	—	—	—	29,882	—	—	—	—	—
Retirement of treasury shares	—	—	—	—	—	—	(29,882)	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	—	—	—	—	7,350	—	—	7,350
Unrealized loss on marketable securities	—	—	—	—	—	—	—	—	—	(2)	—	(2)
Net loss	—	—	—	—	—	—	—	—	—	—	(70,819)	(70,819)
Balance at December 31, 2020	—	\$ —	—	\$ —	27,941,566	\$ 28	—	\$ —	\$ 316,775	\$ (2)	\$ (221,620)	\$ 95,181

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,	
	2020	2019
Operating activities		
Net loss	\$ (70,819)	\$ (82,677)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation expense	2,379	2,053
Stock-based compensation expense	7,350	4,224
In-process research and development expense	—	25,591
Net amortization of premiums and discounts on marketable securities	(68)	—
Changes in operating assets and liabilities:		
Accounts receivable	(2,000)	—
Unbilled accounts receivable	(531)	—
Prepaid expenses and other current assets	(697)	(2,459)
Other assets	(519)	(20)
Accounts payable	1,773	803
Accrued expenses and other liabilities	1,976	2,949
Deferred revenue	7,881	10,000
Deferred rent and deferred lease incentive	(380)	53
Net cash used in operating activities	\$ (53,655)	\$ (39,483)
Investing activities		
Purchases of marketable securities	(124,270)	—
Maturities of marketable securities	68,474	—
Purchases of property and equipment	(1,342)	(853)
Transaction costs associated with asset acquisition	—	(91)
Net cash used in investing activities	(57,138)	(944)
Financing activities		
Payment of Series B convertible preferred stock issuance costs	—	(34)
Proceeds from initial public offering of common stock, net of underwriting discounts and commissions	(193)	64,173
Proceeds from issuance of common stock in connection with private placement, net of issuance costs	64,210	—
Proceeds from issuance of common stock in connection with at-the-market offering, net of issuance costs	5,736	—
Principal payments on capital lease obligations	(50)	(45)
Proceeds from issuance of common stock under benefit plans, net	1,429	249
Net cash provided by financing activities	71,132	64,343
Net (decrease) increase in cash, cash equivalents and restricted cash	(39,661)	23,916
Cash, cash equivalents, and restricted cash, beginning of period	97,805	73,889
Cash, cash equivalents, and restricted cash, end of period	\$ 58,144	\$ 97,805
Supplemental cash flow information		
Cash paid for interest	\$ 4	\$ 7
Non-cash investing and financing activities:		
Acquisition of in process research and development through issuance of stock	\$ —	\$ 25,500
Conversion of convertible preferred stock into common stock	\$ —	\$ 165,136
Property and equipment purchases unpaid at end of period	\$ 262	\$ 34
Public offering costs unpaid at end of period	\$ —	\$ 301

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, 2020	December 31, 2019
Cash and cash equivalents	\$ 57,052	\$ 96,713
Restricted cash	1,092	1,092
Total cash, cash equivalents, and restricted cash	\$ 58,144	\$ 97,805

The accompanying notes are an integral part of these 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 rare diseases in areas of high unmet medical need.

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 generally accepted accounting principles 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”).

Sales of Common Stock

On July 22, 2019, the Company completed an initial public offering (“IPO”) of its common stock and issued and sold 4,500,000 shares of common stock at a public offering price of \$16.00 per share, resulting in net proceeds of \$63.9 million after deducting underwriting discounts and commissions and offering expenses. Upon the closing of the IPO, all 112,500,000 shares of outstanding preferred stock automatically converted into 16,071,418 shares of common stock.

On July 5, 2019, in connection with the IPO, the Company effected a one-for-seven reverse stock split of the Company’s issued and outstanding shares of common stock and a proportional adjustment to the existing conversion ratios for each of the Company’s outstanding series of preferred stock. All share and per share amounts in the accompanying consolidated financial statements and notes thereto for periods prior to the reverse stock split have been retroactively adjusted to give effect to this reverse stock split, including reclassifying an amount equal to the reduction in par value of common stock to additional paid-in capital.

On June 9, 2020, the Company issued and sold 4,029,411 shares of common stock to investors in a private placement at a price of \$17.00 per share, resulting in net proceeds of \$64.3 million after deducting offering costs.

On August 11, 2020, the Company entered into an Equity Distribution Agreement with Piper Sandler & Co. (“Piper Sandler”), as sales agent, pursuant to which the Company may offer and sell shares of its common stock with an aggregate offering price of up to \$75.0 million under an “at-the-market” offering program (the “ATM Offering”). The Equity Distribution Agreement provides that Piper Sandler will be entitled to a sales commission equal to 3.0% of the gross sales price per share of all shares sold under the ATM Offering. From the initiation of the ATM Offering through December 31, 2020, the Company has issued and sold 550,000 shares under the ATM Offering, resulting in aggregate net proceeds of \$5.7 million after deducting issuance costs of \$0.2 million.

On January 22, 2021, the Company completed a public offering of its common stock and issued and sold 4,600,000 shares of common stock at a public offering price of \$11.00 per share, resulting in net proceeds of \$46.4 million after deducting underwriting discounts and commissions and estimated offering expenses.

Liquidity

The Company has incurred recurring losses and negative cash flows from operations since inception and has primarily funded its operations with proceeds from the sale of shares of common stock in public offerings, a private placement, and the ATM Offering, through issuances of convertible preferred stock, and from upfront payments received from the collaboration and license agreements with Acceleron Pharma Inc. (“Acceleron”) and MyoKardia, Inc. (“MyoKardia”), a wholly-owned subsidiary of Bristol Myers Squibb Company. As of December 31, 2020, the Company had an accumulated deficit of \$221.6 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. The Company expects to finance its future cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements.

As of the date of issuance of these financial statements, the Company expects that its cash, cash equivalents, and marketable securities, together with the net proceeds from the sale of its common stock in a public offering on January 22, 2021 of \$46.4 million, will be sufficient to fund its operating expenses and capital expenditure requirements for at least twelve months from the date of issuance of these financial statements. However, the Company has based this estimate on assumptions that may prove to be wrong, and its operating plan may change as a result of many factors currently unknown to it. As a result, the Company could deplete its capital resources sooner than it currently expects. If the Company is unable to raise additional funds through equity or debt financings when needed, it may be required to delay, limit, reduce or terminate development or future commercialization efforts or grant rights to develop and market product candidates that it would otherwise prefer to develop and market itself.

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 revenue recognition, accrued expenses, stock-based compensation expense, the fair value of the Company’s common stock and convertible preferred stock prior to the completion of the IPO, 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.

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 funds that invest in U.S. Treasury obligations. The Company maintains its bank accounts at major financial institutions.

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 and marketable securities are carried at fair value and are classified according to the fair value hierarchy described above (Note 3). The cash equivalents and marketable securities are initially valued at the transaction price, and subsequently revalued at the end of each reporting period, utilizing third-party pricing services. The pricing services utilize industry standard valuation models, including both income and market-based approaches, to determine fair value.

Marketable Securities

The Company classifies securities with a remaining maturity when purchased of greater than three months as marketable securities. As of December 31, 2020, the Company's marketable securities consisted of investments in corporate bonds and commercial paper. Marketable securities are classified as current assets on the consolidated balance sheets if the marketable securities are available to be converted into cash to fund current operations.

Marketable securities are carried at fair value with the unrealized gains and losses included in accumulated other comprehensive loss, which is a component of stockholders' equity, until such gains and losses are realized. Any premium arising at purchase is amortized to interest expense (a component of other income, net) over the period of the earliest call date, and any discount arising at purchase is accreted to interest income (a component of other income, net) over the life of the instrument. Realized gains and losses are determined using the specific identification method and are included in other income, net.

If any adjustment to fair value reflects a decline in value of the investment, the Company considers all available evidence to evaluate the extent to which the decline is "other-than-temporary" and, if so, marks the investment to market through a charge to the Company's statement of operations and comprehensive loss.

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:

	Estimated Useful Life (in years)
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 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, 2020 and 2019.

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.

Revenue Recognition

Under ASC 606, *Revenue from Contracts with Customers*, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. In applying ASC 606, the Company performs the following five steps:

1) Identify the contract with the customer

A contract with a customer exists when (i) the Company enters into an enforceable contract with a customer that defines each party's rights regarding the goods or services to be transferred and identifies the related payment terms, (ii) the contract has commercial substance and (iii) the Company determines that collection of substantially all consideration for goods and services that are transferred is probable based on the customer's intent and ability to pay the promised consideration.

2) Identify the promises and performance obligations in the contract

Performance obligations promised in a contract are identified based on the goods and services that will be transferred to the customer that are both capable of being distinct, whereby the customer can benefit from the good or service either on its own or together with other readily available resources, and are distinct in the context of the contract, whereby the transfer of the good or service is separately identifiable from other promises in the contract. To the extent a contract includes multiple promised goods and services, the Company must apply judgment to determine whether promised goods and services are capable of being distinct and distinct in the context of the contract. In assessing whether a promised good or service is distinct, the Company considers factors such as the research, manufacturing and commercialization capabilities of the customer and the availability of the associated expertise in the marketplace. The Company also considers the intended benefit of the contract in assessing whether a promised good or service is separately identifiable from other promises in the contract. If these criteria are not met, the promised goods and services are accounted for as a combined performance obligation.

3) Determine the transaction price

The transaction price is determined based on the consideration to which the Company will be entitled in exchange for transferring goods and services to the customer. If the consideration promised in a contract includes a variable amount, the Company estimates the amount of consideration to which it will be entitled in exchange for transferring the promised goods or services to a customer. The Company determines the amount of variable consideration by using the expected value method or the most likely amount method. The Company includes the unconstrained amount of estimated variable consideration in the transaction price. The amount included in the transaction price is constrained to the amount for which it is probable that a significant reversal of cumulative revenue recognized will not occur. At the end of each subsequent reporting period, the Company re-evaluates the estimated variable consideration included in the transaction price and any related constraint, and if necessary, adjusts the estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis in the period of adjustment. Changes to the constraint of variable consideration can have a material effect on the amount of revenue recognized in the period.

If an arrangement includes research and development milestone payments, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are based on the occurrence of events not within the Company's control, such as regulatory approvals, are generally not considered probable of being achieved until the underlying events occur or the associated approvals are received.

For arrangements with licenses of intellectual property that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes royalty revenue and sales-based milestones at the later of (i) when the related sales occur, or (ii) when the performance obligation to which the royalty has been allocated has been satisfied.

In determining the transaction price, the Company adjusts consideration for the effects of the time value of money if the timing of payments provides the Company with a significant benefit of financing. The Company assesses its revenue generating arrangements in order to determine whether a significant financing component exists.

4) Allocate the transaction price to the performance obligations in the contract

If the contract contains a single performance obligation, the entire transaction price is allocated to the single performance obligation. Contracts that contain multiple performance obligations require an allocation of the transaction price to each performance obligation on a relative standalone selling price basis, except for any variable consideration that meets the criteria to be allocated entirely to a single performance obligation or to a distinct service that forms part of a single performance obligation.

5) Recognize revenue when or as the Company satisfies a performance obligation

The Company may satisfy performance obligations over time or at a point in time, depending on the nature of the performance obligation. Revenue is recognized over time if the customer simultaneously receives and consumes the benefits provided by the entity's performance, the entity's performance creates or enhances an asset that the customer controls as the asset is created or enhanced, or the entity's performance does not create an asset with an alternative use to the entity and the entity has an enforceable right to payment for performance completed to date. If the entity does not satisfy a performance obligation over time, the related performance obligation is satisfied at a point in time by transferring the control of a promised good or service to a customer.

For revenue that the Company recognizes over time, the Company assesses whether an input or an output method is the appropriate measure of progress associated with the satisfaction of the performance obligation. In determining the appropriate method for measuring progress, the Company considers the nature of the good or service that it has promised to transfer to the customer. Output methods recognize revenue on the basis of direct measurements of the value to the customer of the goods or services transferred to date relative to the remaining goods or services promised under the contract. Input methods recognize revenue on the basis of the entity's efforts or inputs to the satisfaction of a performance obligation. Estimates inherent to the measurement of progress associated with the satisfaction of performance obligations based on an input method include the total estimated costs to satisfy the associated performance obligation.

See Note 10, "Collaboration and License Agreements", for further information on the application of ASC 606 to the collaboration and license agreement with Acceleron (the "Acceleron Collaboration Agreement") and the collaboration and license agreement with MyoKardia (the "MyoKardia Collaboration Agreement").

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. 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.

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 or the extent of services provided during the reporting periods, 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") issued prior to the completion of the IPO 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 initial public offering, 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 prior to the completion of the IPO included the guideline public company method and/or the precedent transaction method to estimate the equity value, and the option-pricing method or the hybrid method, which is a probability-weighted expected return method, 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 prior to the completion of the IPO. 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 associated with 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.

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. 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, 2020 and 2019, comprehensive loss consists of net loss and unrealized losses on investments.

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, marketable securities, 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. The Company's marketable securities primarily consist of corporate bonds and commercial paper, and potentially subject the Company to concentrations of credit risk. The Company has adopted an investment policy that limits the amounts the Company may invest in any one type of investment. The Company has not experienced any credit losses and does not believe it is exposed to any significant credit risk on these funds.

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.

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 March 2017, the FASB issued ASU No. 2017-08, *Receivables - Nonrefundable Fees and Other Costs (Subtopic 310-20): Premium Amortization on Purchased Callable Debt Securities* ("ASU 2017-08"). This standard amends the amortization period for certain purchased callable debt securities held at a premium by shortening the amortization period to the earliest call date. The new standard became effective for the Company on January 1, 2020. The adoption of this standard did not have a material impact on the Company's consolidated financial statements or footnote disclosures.

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 480 with a scope exception and does not impact the accounting for these mandatorily redeemable instruments. The new standard became effective for the Company on January 1, 2020 under the extended transition period. The adoption of this standard did not have a material impact on the Company's consolidated financial statements or footnote disclosures.

In November 2018, the FASB issued ASU No. 2018-18, *Collaborative Arrangements (Topic 808): Clarifying the Interaction between Topic 808 and Topic 606*. The standard clarifies that certain transactions between collaborative arrangement participants should be accounted for as revenue under ASC 606 when the collaborative arrangement participant is a customer in the context of a unit-of-account. The standard amends ASC 808 to refer to the unit-of-account guidance in ASC 606 and requires it to be used only when assessing whether the collaborative arrangement or a part of the arrangement is within the scope of ASC 606. The standard requires that collaborative arrangement revenue not within the scope of ASC 606 be presented separately from revenues from transactions within the scope of ASC 606. The new standard became effective for the Company on January 1, 2020. 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): 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. In November

2019, the FASB deferred the effective date of ASU 2016-02, as amended, for private companies to fiscal years beginning after December 15, 2020. In June 2020, the FASB further deferred the effective date of ASU 2016-02, as amended, for private companies to fiscal years beginning after December 15, 2021. The new standard will become effective for the Company on January 1, 2022. The Company will apply the transition method permitted by ASU 2016-02, as amended. 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, 2023. The Company is currently evaluating the potential impact that this standard may have on its consolidated financial position and results of operations.

In December 2019, the FASB issued ASU No. 2019-12, *Income Taxes—Simplifying the Accounting for Income Taxes* ("ASU 2019-12"). The standard eliminates certain exceptions related to the approach for intraperiod tax allocation, the methodology for calculating income taxes in an interim period, and the recognition of deferred tax liabilities for outside basis differences. The new guidance also simplifies aspects of the accounting for franchise taxes and enacted changes in tax laws or rates and clarifies the accounting for transactions that result in a step-up in the tax basis of goodwill. The new standard will be effective for the Company on January 1, 2023. The Company is currently evaluating the potential impact that this standard may have on its consolidated financial position and results of operations.

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 fair value hierarchy classification of such fair values as of December 31, 2020 and 2019 (in thousands):

	Fair Value Measurements at December 31, 2020			
	Total	Level 1	Level 2	Level 3
Cash equivalents:				
Money market funds	\$ 57,052	\$ 57,052	\$ —	\$ —
Marketable securities:				
Corporate bonds	23,339	—	23,339	—
Commercial paper	32,523	—	32,523	—
Total	<u>\$ 112,914</u>	<u>\$ 57,052</u>	<u>\$ 55,862</u>	<u>\$ —</u>
	Fair Value Measurements at December 31, 2019			
	Total	Level 1	Level 2	Level 3
Cash equivalents:				
Money market funds	\$ 96,713	\$ 96,713	\$ —	\$ —
Total	<u>\$ 96,713</u>	<u>\$ 96,713</u>	<u>\$ —</u>	<u>\$ —</u>

There were no transfers between fair value levels during the years ended December 31, 2020 or 2019.

4. Marketable Securities

Marketable securities consisted of the following as of December 31, 2020 (in thousands):

	Fair Value Measurements at December 31, 2020			Fair Value
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	
Cash equivalents:				
Money market funds	\$ 57,052	\$ —	\$ —	\$ 57,052
Total cash equivalents	57,052	—	—	57,052
Marketable securities:				
Corporate bonds	23,341	2	(4)	23,339
Commercial paper	32,523	—	—	32,523
Total marketable securities	55,864	2	(4)	55,862
Total cash equivalents and marketable securities	\$ 112,916	\$ 2	\$ (4)	\$ 112,914

The Company did not hold any marketable securities as of December 31, 2019.

There were no sales of marketable securities during the year ended December 31, 2020. As of December 31, 2020, the aggregate fair value of securities that were in an unrealized loss position for less than twelve months was \$13.4 million.

The Company determined that it did not hold any securities with any other-than-temporary impairment as of December 31, 2020. As of December 31, 2020, the fair value and amortized cost of securities with a remaining contractual maturity of greater than one year was \$3.1 million. As of December 31, 2020, the Company did not intend to sell, and would not be more likely than not required to sell, the securities in an unrealized loss position before recovery of their amortized cost bases.

5. Property and Equipment, Net

Property and equipment, net consisted of the following (in thousands):

	December 31, 2020	December 31, 2019
Lab equipment	\$ 6,877	\$ 5,710
Furniture and fixtures	594	548
Computer equipment	373	512
Software	199	90
Leasehold improvements	6,210	6,210
Construction in process	262	82
Total property and equipment	14,515	13,152
Less: accumulated depreciation	(6,118)	(3,947)
Property and equipment, net	\$ 8,397	\$ 9,205

Depreciation expense for the years ended December 31, 2020 and 2019 was \$2.4 million and \$2.1 million, respectively. Total property and equipment, gross, as of each of December 31, 2020 and 2019 included \$0.2 million of property and equipment recorded under capital leases. Accumulated depreciation, as of December 31, 2020 and 2019, included \$0.2 million and \$0.1 million, respectively, for property and equipment recorded under capital leases.

6. Additional Balance Sheet Detail

Prepaid expenses and other current assets consisted of the following (in thousands):

	December 31, 2020	December 31, 2019
Prepaid expenses	\$ 3,668	\$ 2,796
Prepaid sign-on bonuses subject to vesting provisions	147	179
Interest income receivable	176	111
Other	74	284
Total prepaid expenses and other current assets	<u>\$ 4,065</u>	<u>\$ 3,370</u>

Accrued expenses and other current liabilities consisted of the following (in thousands):

	December 31, 2020	December 31, 2019
External research and development	\$ 4,082	\$ 2,250
Payroll and benefits	2,928	2,239
Professional services	196	891
Capital lease obligation, current portion	17	50
Restricted stock liability, current portion	6	17
Other	38	49
Total accrued expenses and other current liabilities	<u>\$ 7,267</u>	<u>\$ 5,496</u>

Future minimum lease payments associated with the Company's capital lease obligations are less than \$0.1 million in the year ending December 31, 2021. No minimum lease payments associated with the Company's capital lease obligations are due after December 31, 2021.

7. Preferred Stock

In July 2016, the Company entered into a Series A convertible preferred stock purchase agreement, pursuant to which the Company sold 55,000,000 shares of Series A convertible preferred stock (the "Series A Preferred Stock") at a price of \$1.00 per share. In April 2017, the Company entered into an additional Series A Preferred Stock purchase agreement, pursuant to which the Company sold 5,000,000 shares of Series A Preferred Stock at a price of \$1.00 per share.

In August 2018, the Company entered into a Series B convertible preferred stock purchase agreement, pursuant to which the Company sold 40,000,000 shares of the Series B Preferred Stock at a purchase price of \$2.00 per share. During the year ended December 31, 2019, the Company issued 12,500,000 shares of Series B Preferred Stock in connection with the right of reference and license agreement, as amended, entered into with subsidiaries of GlaxoSmithKline plc (collectively referred to as "GSK") (the "GSK Agreement") (Note 11). 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.

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 was redeemable upon the occurrence of a Deemed Liquidation Event (as defined below), the Preferred Stock was classified outside of stockholders' equity. Since the Preferred Stock was not initially redeemable and the Company determined that it was not probable that it would be redeemable, the carrying value of the Preferred Stock was not adjusted.

On July 5, 2019, the Company eliminated the gross proceeds threshold of \$45.0 million for a firm-commitment underwritten public offering in order to effect an automatic conversion of all outstanding shares of Preferred Stock into common stock upon the closing of the IPO.

Upon the completion of the IPO on July 22, 2019, all 112,500,000 shares of outstanding Preferred Stock automatically converted into 16,071,418 shares of common stock. In addition, upon the completion of the IPO, the Company amended and restated its certificate of incorporation to authorize 5,000,000 shares of preferred stock, which shares of preferred stock are currently undesignated. As of December 31, 2020 and 2019, 5,000,000 shares of undesignated preferred stock were authorized and no shares of preferred stock were issued or outstanding.

Prior to the closing of the IPO, the holders of the Preferred Stock had the following rights, privileges, and preferences:

Voting Rights

The holders of the Preferred Stock were entitled to vote on all matters submitted to stockholders for a vote and had 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 voted 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, were entitled to elect one director of the Company and the holders of Series B Preferred Stock, exclusively and as a separate class, were entitled to elect one director of the Company.

Conversion

Each share of Preferred Stock was 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 Preferred Stock in effect at the time of conversion. The Original Issue Price was \$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 was \$7.00 per share for Series A Preferred Stock and \$14.00 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 would have been automatically converted 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"), and, following such offering, the common stock was 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 approved a mandatory conversion in connection with a proposed Deemed Liquidation Event in which the holders of Series B Preferred Stock would have received less than the full liquidation preference applicable to the Series B Preferred Stock (as discussed below), then the mandatory conversion would have also required 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 accrued 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 accrued 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 were cumulative and were 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 could not declare dividends on the common stock unless the holders of Preferred Stock first received, or simultaneously received, 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 would have been entitled to be paid out of the assets of the Company available for distribution to its stockholders before any payment was 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 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 would have been 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, elected otherwise, a “Deemed Liquidation Event” included (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.

8. Common Stock

As of December 31, 2020, the Company’s restated certificate of incorporation authorized the Company to issue 200,000,000 shares of common stock, \$0.001 par value per share.

Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company’s stockholders. Common stockholders are not entitled to receive dividends, unless declared by the Company’s board of directors, subject to the preferential dividend rights of any preferred stock then outstanding. No dividends have been declared or paid by the Company since its inception.

As of December 31, 2020 and 2019, the Company has reserved for future issuance the following number of shares of common stock:

	<u>December 31,</u> <u>2020</u>	<u>December 31,</u> <u>2019</u>
Shares reserved for exercises of outstanding stock options	2,962,347	2,023,828
Shares reserved for future issuance under the 2019 Stock Incentive Plan	1,728,616	1,866,694
Shares reserved for future issuance under the 2019 Employee Stock Purchase Plan	465,999	252,142
	<u>5,156,962</u>	<u>4,142,664</u>

9. Stock-based Compensation Expense

2016 Stock Incentive Plan

In July 2016, the Company adopted the 2016 Stock Incentive Plan (the “2016 Plan”), which provided for the grant of restricted stock awards, restricted stock units, incentive stock options, non-statutory stock options, and other stock-based awards to the Company’s eligible employees, officers, directors, consultants, and advisors. As of the effective date of the 2019 Stock Incentive Plan (the “2019 Plan”), and as of December 31, 2020 and 2019, no shares remained available for future issuance under the 2016 Plan. Any options or awards outstanding under the 2016 Plan remain outstanding and effective.

2019 Stock Incentive Plan

On July 2, 2019, the Company's stockholders approved the 2019 Plan, which became effective on July 17, 2019. 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 to the Company's officers, employees, directors, consultants and advisors. The number of shares initially reserved for issuance under the 2019 Plan was 2,017,142 shares, plus the shares of common stock remaining available for issuance under the 2016 Plan as of July 17, 2019. The number of shares reserved will be annually increased on January 1, 2020 and each January 1 thereafter through January 1, 2029 by the least of (i) 2,000,000 shares, (ii) 4% of the number of shares of the Company's common stock outstanding on the first day of each such year or (iii) an amount determined by the Company's board of directors. As of December 31, 2020, there were 1,728,616 shares available for future issuance under the 2019 Plan. On January 1, 2021, the number of shares reserved for issuance under the 2019 Plan was increased by 1,122,696 shares.

The shares of common stock underlying any awards that expire, terminate, or are otherwise surrendered, cancelled, forfeited or repurchased by the Company under the 2016 Plan or the 2019 Plan will be added back to the shares of common stock available for issuance under the 2019 Plan. As of July 17, 2019, no further awards will be made under the 2016 Plan.

For financial reporting purposes, the Company performed common stock valuations with the assistance of a third-party specialist as of May 10, 2019, 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. Following the completion of the IPO, the fair value of the common stock on the grant date was based on the closing price of the stock on the Nasdaq Global Market on the date of grant.

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. 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. Shares issued upon the exercise of stock options are issued from the Company's pool of authorized but unissued common stock.

The shares of common stock underlying restricted stock awards typically vest over a four-year period. The shares of common stock are recorded in stockholders' equity as they vest.

The following table summarizes the Company's restricted stock activity under the 2019 Plan and 2016 Plan since December 31, 2018:

	Number of Shares	Weighted Average Grant Date Fair Value
Unvested at December 31, 2018	757,022	\$ 3.07
Granted	—	—
Vested	(349,149)	3.10
Repurchased	(61,450)	3.02
Unvested at December 31, 2019	346,423	\$ 3.05
Granted	—	—
Vested	(233,563)	3.00
Repurchased	(29,882)	3.05
Unvested at December 31, 2020	<u>82,978</u>	3.19

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 2019 Plan and 2016 Plan during the year ended December 31, 2020:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value
Outstanding at December 31, 2019	2,023,828	\$ 9.31	9.12	\$ 14,840,035
Granted	1,352,306	14.60		
Exercised	(162,861)	7.49		
Cancelled	(250,926)	12.30		
Outstanding at December 31, 2020	2,962,347	\$ 11.57	8.55	\$ 5,767,895
Exercisable at December 31, 2020	873,748	\$ 10.54	7.98	\$ 2,256,315

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 years ended December 31, 2020 and 2019 was \$9.76 per share and \$6.97 per share, respectively. The total intrinsic value of stock options exercised in the years ended December 31, 2020 and 2019 was \$1.4 million and \$0.2 million, respectively.

The fair value of stock options granted during the years ended December 31, 2020 and 2019 under the 2019 Plan and 2016 Plan has been calculated on the date of grant using the following weighted average assumptions:

	Year Ended December 31, 2020	Year Ended December 31, 2019
Risk-free interest rate	1.2%	2.3%
Expected dividend yield	0.0%	0.0%
Expected term (years)	6.0	6.0
Expected stock price volatility	77.6%	80.9%

Grants Outside of the 2016 Stock Incentive Plan and the 2019 Stock Incentive Plan

The following table summarizes the Company's restricted stock activity outside of the 2019 Plan and 2016 Plan since December 31, 2018:

	Number of Shares	Weighted Average Grant Date Fair Value
Unvested at December 31, 2018	446,789	\$ 2.94
Granted	—	—
Vested	(112,142)	2.94
Repurchased	—	—
Unvested at December 31, 2019	334,647	\$ 2.94
Granted	—	—
Vested	(291,789)	2.94
Repurchased	—	—
Unvested at December 31, 2020	42,858	\$ 2.93

The aggregate intrinsic value of all restricted stock awards that vested during the years ended December 31, 2020 and 2019 was \$8.8 million and \$4.8 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,	
	2020	2019
General and administrative	\$ 3,970	\$ 1,977
Research and development	3,380	2,247
Total stock-based compensation expense	<u>\$ 7,350</u>	<u>\$ 4,224</u>

As of December 31, 2020, the Company had an aggregate of \$16.0 million of unrecognized stock-based compensation expense, which is expected to be recognized over a weighted average period of 2.57 years.

2019 Employee Stock Purchase Plan

On July 2, 2019, the Company's stockholders approved the 2019 Employee Stock Purchase Plan (the "ESPP"), which became effective on July 17, 2019. A total of 252,142 shares of common stock were initially reserved for issuance under the ESPP. In addition, the number of shares of common stock reserved under the ESPP will be annually increased on January 1, 2020, and each January 1 thereafter through January 1, 2029, by the least of (i) 428,571 shares of common stock, (ii) 1% of the number of shares of the Company's common stock outstanding on the first day of each such year or (iii) an amount determined by the Company's board of directors. As of December 31, 2020, there were 465,999 shares available for future issuance under the ESPP. On January 1, 2021, the number of shares reserved for issuance under the 2019 ESPP was increased by 280,674 shares.

10. Collaboration and License Agreements

Accelaron Collaboration Agreement

On December 20, 2019, the Company entered into the Accelaron Collaboration Agreement to identify biological targets to modulate specific pathways associated with a targeted indication within the pulmonary disease space (the "Indication"). Under the terms of the Accelaron Collaboration Agreement, the Company granted Accelaron an exclusive worldwide license under certain intellectual property rights to make, have made, use, sell, have sold, import, export, distribute and have distributed, market, have marketed, promote, have promoted, or otherwise exploit molecules and products directed against or expressing certain biological targets identified by the Company for the treatment, prophylaxis, or diagnosis of the Indication.

Pursuant to a mutually agreed research plan, the Company will perform assay screening and related research activities to identify and validate potential biological targets for further research, in order to support the development, manufacture and commercialization of product candidates by Accelaron. Upon completion of the research activities, the Company will deliver a data package to Accelaron with respect to the biological targets identified by the Company in the conduct of the research activities for the treatment, prophylaxis, or diagnosis of the Indication. As provided for under the exclusive worldwide license that was conveyed at the inception of the arrangement, Accelaron has the right to designate a specified number of the biological targets identified by the Company for Accelaron's research, development, manufacture and commercialization of products or molecules directed to such targets for the treatment, prophylaxis, or diagnosis of the Indication (the "Targets"). If Accelaron does not designate any Targets during the designated period, then the Accelaron Collaboration Agreement will automatically terminate. If Accelaron designates one or more Targets, then Accelaron will be obligated to use commercially reasonable efforts to seek regulatory approval for one product directed to a Target in certain specified countries. Upon receipt of regulatory approval for any product directed to a Target, Accelaron must use commercially reasonable efforts to commercialize such product in certain specified countries.

Accelaron may also request that the Company perform medicinal chemistry services related to the generation and optimization of molecules directed against or expressing biological targets for the treatment, prophylaxis, or diagnosis of the Indication beyond the scope of the research plan. If the Company agrees to provide such medicinal chemistry services, the Company and Accelaron will negotiate to determine the scope, timeline and budget for such medicinal chemistry services.

The Company received a non-refundable upfront payment of \$10.0 million in December 2019 upon the execution of the Accelaron Collaboration Agreement. The Company is entitled to research milestone payments of up to \$18.5 million in the aggregate upon achievement of specified research milestones, development milestone payments of up to \$202.5 million in

the aggregate upon achievement of specified clinical and regulatory milestones, and sales milestones payments of up to \$217.5 million in the aggregate upon the achievement of certain aggregate annual worldwide net sales milestones for certain products directed to a Target that have achieved such milestones. To date, the Company achieved \$2.0 million of specified research milestones. In addition, the Company is entitled to tiered royalties ranging from a mid single-digit percentage to a low double-digit percentage on Acceleron's annual worldwide net sales of products directed to any Target, subject to reduction in specified circumstances. The Company is also entitled to receive reimbursement from Acceleron for research costs incurred under the research plan, including internal and external costs.

The Acceleron Collaboration Agreement continues on a country-by-country and Target-by-Target basis until the last to expire royalty term for a product directed to such Target, at which time the Acceleron Collaboration Agreement expires with respect to such Target in such country. Either party has the right to terminate the Acceleron Collaboration Agreement if the other party has materially breached in the performance of its obligations under the contract and such breach has not been cured within the applicable cure period. Acceleron also has the right to terminate the Acceleron Collaboration Agreement for convenience in its entirety or on a Target-by-Target and, if the Company performs medicinal chemistry services, on a molecule-by-molecule basis with respect to any molecule directed against a Target.

While the Company is performing the research activities pursuant to the research plan and for a specified period thereafter, the Company may not research, develop, manufacture, commercialize, use, or otherwise exploit any compound or product for the treatment, prophylaxis, or diagnosis of the Indication other than for Acceleron. While the Company is performing the research activities pursuant to the research plan and for a specified period thereafter, other than for Acceleron, the Company may not research, develop, manufacture, commercialize, use, or otherwise exploit any compound or product for the treatment, prophylaxis, or diagnosis of the Indication that is directed against certain specified biological targets identified by the Company in the performance of the research activities.

Accounting Analysis

Identification of the Contract

The Company assessed the Acceleron Collaboration Agreement and concluded that it represents a contract with a customer within the scope of ASC 606.

Identification of the Promises and Performance Obligations

The Company determined that the Acceleron Collaboration Agreement contains the following promises: (i) an exclusive worldwide license under certain intellectual property rights, including rights to a specified number of biological targets identified by the Company for the treatment, prophylaxis, or diagnosis of a targeted indication within the pulmonary disease space that was conveyed at the inception of the arrangement (the "License"), (ii) research services to identify and validate potential biological targets (the "Research Services"), and (iii) participation in the joint steering committee (the "JSC").

The Company assessed the above promises and concluded that the License is not capable of being distinct from the Research Services given that the License has limited value without the performance of the Research Services and the Research Services can only be performed by the Company due to their specialized nature. Therefore, the Company has concluded that the License and the Research Services represent a single combined performance obligation.

The Company also assessed the participation on the JSC and concluded that the promise is quantitatively and qualitatively immaterial in the context of the Acceleron Collaboration Agreement. Accordingly, the Company has disregarded its participation on the JSC as a performance obligation.

The potential medicinal chemistry services were not identified as a promised good or service because the Company is under no obligation to provide those services.

Determination of the Transaction Price

The Company received a non-refundable upfront payment of \$10.0 million upon the execution of the Acceleron Collaboration Agreement, which the Company included in the transaction price. In December 2020, the Company achieved \$2.0 million of specified research milestones associated with the Acceleron Collaboration Agreement, which were previously constrained due to the significant uncertainty regarding whether such research milestones would be achieved. The Company included this amount in the transaction price as of December 31, 2020. Based on the continued uncertainty associated with the achievement of any of the remaining research and development milestone payments that the Company is eligible to receive, the Company has constrained the variable consideration associated with those remaining milestone payments and excluded them from the transaction price. As part of its evaluation of constraining the research and development milestones, the Company considered numerous factors, including the fact that the achievement of the research and development milestones are contingent upon the results of the underlying research and development activities and are thus outside of the control of the Company.

The Company also included in the transaction price the expected amount of costs to be reimbursed for the Research Services.

The Company will reassess the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur, and, if necessary, adjust its estimate of the transaction price.

Any consideration related to sales milestone payments (including royalties) will be recognized when the related sales occur as these amounts have been determined to relate predominantly to the license granted to Acceleron and therefore are recognized at the later of when the related sales occur or the performance obligation is satisfied.

Allocation of the Transaction Price to Performance Obligations

As noted above, the Company has identified a single performance obligation associated with the Acceleron Collaboration Agreement. Therefore, the Company will allocate the entire amount of the transaction price to the identified single performance obligation.

Recognition of Revenue

The Company recognizes revenue related to the Acceleron Collaboration Agreement over time as the Research Services are rendered. The Company has concluded that an input method is a representative depiction of the transfer of services under the Acceleron Collaboration Agreement. The method of measuring progress towards the delivery of the services incorporates actual cumulative internal and external costs incurred relative to total internal and external costs expected to be incurred to satisfy the performance obligation. The period over which total costs are estimated reflects the Company's estimate of the period over which it will perform the Research Services. Changes in estimates of total internal and external costs expected to be incurred are recognized in the period of change as a cumulative catch-up adjustment.

During the year ended December 31, 2020, the Company recognized \$6.3 million of collaboration revenue associated with the Acceleron Collaboration Agreement, which includes a cumulative catch-up adjustment of \$0.5 million attributable to the removal of the constraint associated with the \$2.0 million of research milestones achieved in December 2020, and \$3.4 million of revenue recognized that was included in deferred revenue as of December 31, 2019. During the year ended December 31, 2019, the Company did not recognize any revenue under the Acceleron Collaboration Agreement, as no Research Services had been performed. As of December 31, 2020 and 2019, the Company recorded deferred revenue associated with the Acceleron Collaboration Agreement of \$7.9 million and \$10.0 million, respectively, which is classified as either current or net of current portion in the accompanying consolidated balance sheets based on the period over which the revenue is expected to be recognized. The aggregate deferred revenue balance represents the aggregate amount of the transaction price allocated to the performance obligations that are unsatisfied as of December 31, 2020. As of December 31, 2020, the Company had received \$1.7 million of cost reimbursement payments, and no milestone or royalty payments under the Acceleron Collaboration Agreement. As of December 31, 2019, the Company had not received any milestone, royalty, or cost reimbursement payments under the Acceleron Collaboration Agreement. As of December 31, 2020, the Company recorded unbilled accounts receivable of \$0.5 million related to reimbursable research and development costs under the Acceleron Collaboration Agreement for activities performed during the three months ended December 31, 2020. As of December 31, 2020, the Company recorded accounts receivable of \$2.0 million associated with the achievement of specified research milestones in December 2020. As of December 31, 2019, the Company had recorded no accounts receivable under the Acceleron Collaboration Agreement.

MyoKardia Collaboration Agreement

On July 20, 2020, the Company entered into the MyoKardia Collaboration Agreement, pursuant to which the Company granted to MyoKardia an exclusive worldwide license under certain intellectual property rights to research, develop, make, have made, use, have used, sell, have sold, offer for sale, have offered for sale, import, have imported, export, have exported, distribute, have distributed, market, have marketed, promote, have promoted, or otherwise exploit products directed against certain biological targets identified by the Company that are capable of modulating up to a certain number of genes of interest with relevance to certain genetically defined cardiomyopathies.

Pursuant to a mutually agreed research plan, the Company will perform assay screening and related research activities to identify and validate up to a specified number of potential cardiomyopathy gene targets (“Identified Targets”) for further research, development, manufacture and commercialization by MyoKardia. The Company and MyoKardia will work together to determine how best to advance at each stage of the research activities under the research plan and to identify which of the Identified Targets, if any, meet the criteria set forth in the research plan (the “Cardiomyopathy Target Candidates”). Upon completion of the research plan, the parties will work together to prepare a final data package and MyoKardia may designate certain Cardiomyopathy Target Candidates for MyoKardia’s further exploitation under the MyoKardia Collaboration Agreement (the “Cardiomyopathy Targets”). If MyoKardia does not designate any Cardiomyopathy Targets during the designated period, then the MyoKardia Collaboration Agreement will automatically terminate. If MyoKardia designates one or more Cardiomyopathy Targets, then MyoKardia will be obligated to use commercially reasonable efforts to seek regulatory approval for and to commercialize one product directed against an Identified Target in certain specified countries.

During the period in which the Company is performing the research activities pursuant to the research plan (the “Research Term”) and for a specified period beyond the Research Term if MyoKardia designates a Cardiomyopathy Target, the Company may only use the data generated from such research activities for MyoKardia in accordance with the MyoKardia Collaboration Agreement. During the Research Term and for a specified period thereafter, the Company may not research, develop, manufacture, commercialize, use, or otherwise exploit any compound or product (a) that is a Compound or Product under the MyoKardia Collaboration Agreement that is directed against the Cardiomyopathy Target Candidates for the treatment, prophylaxis, or diagnosis of any indication or (b) for the treatment of any genetically defined cardiomyopathies shown to be related to certain specified genes of interest that are modulated by the Cardiomyopathy Targets.

Under the MyoKardia Collaboration Agreement, MyoKardia made a \$10.0 million upfront payment and a \$2.5 million payment as prepaid research funding to the Company in July 2020. MyoKardia will also reimburse the Company for the costs of the research activities not covered by the prepaid research funding, up to a maximum amount of total research funding (including the prepaid research funding). Upon the achievement of specified preclinical, development and sales milestones, the Company will be entitled to preclinical milestone payments, development milestone payments and sales milestone payments of up to \$298.5 million in the aggregate per target for certain Identified Targets, and of up to \$150.0 million in the aggregate per target for certain other Identified Targets. MyoKardia will also pay the Company tiered royalties ranging from a mid single-digit percentage to a low double-digit percentage based on MyoKardia’s, and any of its affiliates’ and sublicensees’, annual worldwide net sales of products under the MyoKardia Collaboration Agreement directed against any Identified Target. The royalties are payable on a product-by-product basis during a specified royalty term, and may be reduced in specified circumstances.

The MyoKardia Collaboration Agreement continues on a country-by-country and product-by-product basis until the last to expire royalty term for a product, at which time the MyoKardia Collaboration Agreement expires with respect to such product in such country. Either party has the right to terminate the MyoKardia Collaboration Agreement if the other party has materially breached in the performance of its obligations under the MyoKardia Collaboration Agreement and such breach has not been cured within the applicable cure period. MyoKardia also has the right to terminate the MyoKardia Collaboration Agreement for convenience in its entirety or on a target-by-target, product-by-product or molecule-by-molecule basis.

Accounting Analysis

Identification of the Contract

The Company assessed the MyoKardia Collaboration Agreement and concluded that it represents a contract with a customer within the scope of ASC 606.

Identification of the Promises and Performance Obligations

The Company determined that the MyoKardia Collaboration Agreement contains the following promises: (i) an exclusive worldwide license under certain intellectual property rights, including rights to a specified number of potential cardiomyopathy gene targets identified by the Company for further research, development, manufacture and commercialization for the treatment, prophylaxis, or diagnosis of certain genetically defined cardiomyopathies that was conveyed at the inception of the arrangement (the “MyoKardia License”), (ii) research services to identify and validate potential biological targets (the “MyoKardia Research Services”), and (iii) participation in the joint steering committee (the “MyoKardia JSC”).

The Company assessed the above promises and concluded that the MyoKardia License is not capable of being distinct from the MyoKardia Research Services given that the MyoKardia License has limited value without the performance of the MyoKardia Research Services and the MyoKardia Research Services can only be performed by the Company due to their specialized nature. Therefore, the Company has concluded that the MyoKardia License and the MyoKardia Research Services represent a single combined performance obligation.

The Company also assessed the participation on the MyoKardia JSC and concluded that the promise is quantitatively and qualitatively immaterial in the context of the MyoKardia Collaboration Agreement. Accordingly, the Company has disregarded its participation on the MyoKardia JSC as a performance obligation.

Determination of the Transaction Price

The Company received a non-refundable upfront payment of \$10.0 million, which the Company included in the transaction price. Based on the uncertainty associated with the achievement of any preclinical and development milestone payments that the Company is eligible to receive, the Company has constrained the variable consideration associated with those milestone payments and excluded them from the transaction price. As part of its evaluation of constraining the preclinical and development milestones, the Company considered numerous factors, including the fact that the achievement of the preclinical and development milestones are contingent upon the results of the underlying preclinical and development activities and are thus outside of the control of the Company.

The Company also included in the transaction price the expected amount of costs to be reimbursed for the MyoKardia Research Services, which includes the \$2.5 million prepaid research funding payment that the Company received in the third quarter of 2020.

The Company reassesses the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur, and, if necessary, adjusts its estimate of the transaction price.

Any consideration related to sales milestone payments (including royalties) will be recognized when the related sales occur as these amounts have been determined to relate predominantly to the license granted to MyoKardia and therefore are recognized at the later of when the related sales occur or the performance obligation is satisfied.

Allocation of the Transaction Price to Performance Obligations

As noted above, the Company has identified a single performance obligation associated with the MyoKardia Collaboration Agreement. Therefore, the Company will allocate the entire amount of the transaction price to the identified single performance obligation.

Recognition of Revenue

The Company recognizes revenue related to the MyoKardia Collaboration Agreement over time as the MyoKardia Research Services are rendered. The Company has concluded that an input method is a representative depiction of the transfer of services under the MyoKardia Collaboration Agreement. The method of measuring progress towards the delivery of the services incorporates actual cumulative internal and external costs incurred relative to total internal and external costs expected to be incurred to satisfy the performance obligation. The period over which total costs are estimated reflects the Company’s estimate of the period over which it will perform the MyoKardia Research Services. Changes in estimates of total internal and external costs expected to be incurred are recognized in the period of change as a cumulative catch-up adjustment.

During the year ended December 31, 2020, the Company recognized \$2.5 million of collaboration revenue associated with the MyoKardia Collaboration Agreement. During the year ended December 31, 2019, the Company did not recognize any revenue under the MyoKardia Collaboration Agreement as it had not yet entered into the MyoKardia Collaboration

Agreement. As of December 31, 2020, the Company recorded deferred revenue of \$10.0 million associated with the MyoKardia Collaboration Agreement, which is classified as either current or net of current portion in the accompanying consolidated balance sheets based on the period over which the revenue is expected to be recognized. As of December 31, 2019, the Company recorded no deferred revenue associated with the MyoKardia Collaboration Agreement as it had not yet entered into the MyoKardia Collaboration Agreement. The aggregate deferred revenue balance represents the aggregate amount of the transaction price allocated to the performance obligations that are unsatisfied as of December 31, 2020. As of December 31, 2020, the Company had not received any milestone, royalty, or cost reimbursement payments under the MyoKardia Collaboration Agreement, other than the \$2.5 million payment as prepaid research funding in July 2020. As of December 31, 2020, the Company has recorded no accounts receivable related to reimbursable MyoKardia Research Services costs under the MyoKardia Collaboration Agreement.

11. Asset Acquisition

In February 2019, the Company entered into the GSK Agreement, 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 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, including \$2.5 million due upon the initiation of a Phase 2 clinical trial, which was achieved and paid during the third quarter of 2019, 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 Company recorded the \$2.5 million milestone due upon the initiation of a Phase 2 clinical trial as research and development expense in the Company's consolidated statement of operations and comprehensive loss for the year ended December 31, 2019.

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 during the year ended December 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.

12. Commitments and Contingencies

Operating Leases

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 when the Company gained access to the leased space for purposes of making leasehold improvements. 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. 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, 2020 and 2019. 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, 2020 and 2019 was approximately \$1.9 million.

The future minimum lease payments associated with the lease for the Company's current headquarters as of December 31, 2020 are as follows (in thousands):

2021	\$	2,354
2022		2,424
2023		2,497
2024		2,572
2025		2,649
Thereafter		6,966
Total minimum lease payments	\$	<u>19,462</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, 2020, 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, 2020 or 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 for the years ended December 31, 2020 and 2019.

13. 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, 2020	Year Ended December 31, 2019
Federal income tax at statutory rate	21.00%	21.00%
Permanent differences	(0.79)	(0.67)
Federal and state research and development credits	2.57	2.06
Federal orphan drug credits	4.28	—
State income tax, net of federal benefit	6.14	6.16
Other	0.47	0.48
Change in valuation allowance	(33.67)	(29.03)
Effective income tax rate	<u>—%</u>	<u>—%</u>

During the years ended December 31, 2020 and 2019, 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.

The Company's deferred tax assets and liabilities consist of the following (in thousands):

	December 31, 2020	December 31, 2019
Deferred tax assets:		
Net operating loss carryforwards	\$ 46,603	\$ 30,444
Research and development credit carryforwards	6,842	4,658
Orphan drug credit carryforwards	3,032	—
Intangible assets	6,722	7,235
Deferred revenue	1,791	—
Accrued expenses and other	2,240	1,149
Deferred lease incentive	962	1,090
Deferred rent	450	426
Gross deferred tax assets	68,642	45,002
Valuation allowance	(67,427)	(43,586)
Net deferred tax assets	1,215	1,416
Deferred tax liability	(1,215)	(1,416)
Net deferred tax assets	<u>\$ —</u>	<u>\$ —</u>

The Company has evaluated the positive and negative evidence bearing upon its ability to realize the net 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 net deferred tax assets. Accordingly, a full valuation allowance has been established against the net deferred tax assets as of December 31, 2020 and 2019. The valuation allowance increased by \$23.8 million during the year ended December 31, 2020, which is primarily attributable to increases in net operating loss carryforwards as a result of current year net losses and the generation of research and development and orphan drug tax credit carryforwards. The Company reevaluates the positive and negative evidence at each reporting period.

As of December 31, 2020, the Company had federal net operating loss carryforwards of approximately \$170.7 million which begin to expire in 2035. Approximately \$139.7 million of the federal net operating losses can be carried forward indefinitely. As of December 31, 2020, the Company also had state net operating loss carryforwards of approximately \$170.2 million, which begin to expire in 2035.

As of December 31, 2020, the Company had federal orphan drug credits of approximately \$3.0 million, which begin to expire in 2040. As of December 31, 2020, the Company had federal research and development tax credit carryforwards of approximately \$4.6 million, which begin to expire in 2035. As of December 31, 2020, the Company also had state research and development tax credit carryforwards of approximately \$2.8 million, which begin to expire in 2030.

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 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, 2020, the Company’s tax years are still open under statute from 2016 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, 2020 and 2019, 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, 2020, 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.

14. 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.

15. 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:

	Year Ended December 31,	
	2020	2019
Outstanding stock options	2,962,347	2,023,828
Unvested restricted stock awards	125,836	681,070
Total	3,088,183	2,704,898

16. Related-Party Transactions

During the year ended December 31, 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 the year ended December 31, 2019. The Company did not record expenses related to such fees during the year ended December 31, 2020. During the year ended December 31, 2020, the Company did not pay fees to TRV in exchange for services. As of December 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. As of December 31, 2020, there were no amounts due to TRV for such services that were included in accounts payable and accrued expenses. Additionally, consultants that provided services to the Company are employees of TRV. The Company has issued an aggregate of 142,284 shares of common stock to these consultants in exchange for their continuing consulting services.

EXHIBIT INDEX

Exhibit Number	Description
3.1	Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-38978) filed with the Securities and Exchange Commission on July 22, 2019).
3.2	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K (File No. 001-38978) filed with the Securities and Exchange Commission on July 22, 2019).
4.1	Specimen Stock Certificate evidencing shares of common stock (incorporated by reference to Exhibit 4.1 to the Registrant's Registration Statement on Form S-1 (File No. 333-232260) filed with the Securities and Exchange Commission on June 21, 2019).
4.2	Description of the Registrant's Securities Registered under Section 12 of the Exchange Act (incorporated by reference to Exhibit 4.2 to the Registrant's Annual Report on Form 10-K (File No. 001-38978) filed with the Securities and Exchange Commission on March 5, 2020).
10.1	Amended and Restated Investors' Rights Agreement, dated as of August 24, 2018, by and among the Registrant and the other parties thereto (incorporated by reference to Exhibit 10.1 to the Registrant's Registration Statement on Form S-1 (File No. 333-232260) filed with the Securities and Exchange Commission on June 21, 2019).
10.2#	2016 Stock Incentive Plan, as amended (incorporated by reference to Exhibit 10.2 to the Registrant's Registration Statement on Form S-1 (File No. 333-232260) filed with the Securities and Exchange Commission on June 21, 2019).
10.3#	Form of Incentive Stock Option Agreement under the 2016 Stock Incentive Plan (incorporated by reference to Exhibit 10.3 to the Registrant's Registration Statement on Form S-1 (File No. 333-232260) filed with the Securities and Exchange Commission on June 21, 2019).
10.4#	Form of Non-Statutory Stock Option Agreement under the 2016 Stock Incentive Plan (incorporated by reference to Exhibit 10.4 to the Registrant's Registration Statement on Form S-1 (File No. 333-232260) filed with the Securities and Exchange Commission on June 21, 2019).
10.5#	Form of Restricted Stock Agreement under the 2016 Stock Incentive Plan (incorporated by reference to Exhibit 10.5 to the Registrant's Registration Statement on Form S-1 (File No. 333-232260) filed with the Securities and Exchange Commission on June 21, 2019).
10.6#	2019 Stock Incentive Plan (incorporated by reference to Exhibit 10.6 to Amendment No. 1 to Registrant's Registration Statement on Form S-1 (File No. 333-232260) filed with the Securities and Exchange Commission on July 8, 2019).
10.7#	Form of Stock Option Agreement under the 2019 Stock Incentive Plan (incorporated by reference to Exhibit 10.7 to Amendment No. 1 to Registrant's Registration Statement on Form S-1 (File No. 333-232260) filed with the Securities and Exchange Commission on July 8, 2019).
10.8#	2019 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.8 to Amendment No. 1 to Registrant's Registration Statement on Form S-1 (File No. 333-232260) filed with the Securities and Exchange Commission on July 8, 2019).
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 (incorporated by reference to Exhibit 10.10 to the Registrant's Registration Statement on Form S-1 (File No. 333-232260) filed with the Securities and Exchange Commission on June 21, 2019).
10.11	Lease for 26 Landsdowne Street, dated November 22, 2017, by and between the UP 26 Landsdowne, LLC and the Registrant (incorporated by reference to Exhibit 10.11 to the Registrant's Registration Statement on Form S-1 (File No. 333-232260) filed with the Securities and Exchange Commission on June 21, 2019).
10.12#	Form of Employment Agreement for Executive Officers (incorporated by reference to Exhibit 10.12 to Amendment No. 1 to Registrant's Registration Statement on Form S-1 (File No. 333-232260) filed with the Securities and Exchange Commission on July 8, 2019).
10.13#	Employment Agreement, dated June 30, 2019, by and between the Registrant and Robert J. Gould (incorporated by reference to Exhibit 10.13 to Amendment No. 2 to Registrant's Registration Statement on Form S-1 (File No. 333-232260) filed with the Securities and Exchange Commission on July 12, 2019).
10.14#	Employment Agreement, dated July 3, 2019, by and between the Registrant and Bryan Stuart (incorporated by reference to Exhibit 10.14 to Amendment No. 2 to Registrant's Registration Statement on Form S-1 (File No. 333-232260) filed with the Securities and Exchange Commission on July 12, 2019).

10.15#	Employment Agreement, dated July 18, 2019, by and between the Registrant and Owen Wallace (incorporated by reference to Exhibit 10.1 to Registrant's Quarterly Report on Form 10-Q (File No. 001-38978) filed with the Securities and Exchange Commission on May 13, 2020).
10.16*#	Employment Agreement, dated October 29, 2020, by and between the Registrant and Curtis Oltmans.
10.17#	Form of Indemnification Agreement between the Registrant and each of its Executive Officers and Directors (incorporated by reference to Exhibit 10.15 to Registrant's Registration Statement on Form S-1 (File No. 333-232260) filed with the Securities and Exchange Commission on June 21, 2019).
10.18+	Collaboration and License Agreement, dated as of December 20, 2019, by and between the Registrant and Acceleron Pharma Inc (incorporated by reference to Exhibit 10.17 to the Registrant's Annual Report on Form 10-K (File No. 001-38978) filed with the Securities and Exchange Commission on March 5, 2020).
10.19+	Collaboration and License Agreement, dated as of July 20, 2020, by and between the Registrant and MyoKardia, Inc, a wholly-owned subsidiary of Bristol Myers Squibb Company (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-38978) filed with the Securities and Exchange Commission on November 10, 2020).
10.20+	First Amendment to the Right of Reference and License Agreement, dated as of September 23, 2020, by and among the Registrant, GlaxoSmithKline Intellectual Property (No. 2) Limited, GlaxoSmithKline LLC and Glaxo Group Limited (incorporated by reference to Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-38978) filed with the Securities and Exchange Commission on November 10, 2020).
10.21	Securities Purchase Agreement, dated June 9, 2020, by and among the Company and the other parties thereto (incorporated by reference to Exhibit 10.1 of the Company's Current Report on Form 8-K (File No. 001-38978) filed with the Securities and Exchange Commission on June 10, 2020).
10.22	Registration Rights Agreement, dated June 9, 2020, by and among the Company and the other parties thereto (incorporated by reference to Exhibit 10.2 of the Company's Current Report on Form 8-K (File No. 001-38978) filed with the Securities and Exchange Commission on June 10, 2020).
21.1*	Subsidiary of the Registrant.
23.1*	Consent of Ernst & Young LLP, independent registered public accounting firm.
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1+	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2+	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

Indicates a management contract or any compensatory plan, contract or arrangement.

† Certain portions of this exhibit have been omitted because they are not material and would likely cause competitive harm to the Registrant if disclosed.

* Filed herewith.

+ Furnished herewith.

FULCRUM THERAPEUTICS, INC.

NON-EMPLOYEE DIRECTOR COMPENSATION POLICY

Effective January 25, 2021

The Company's non-employee directors shall receive the following compensation for their service as members of the Board of Directors (the "Board") of the Company.

Director Compensation

Our goal is to provide compensation for our non-employee directors in a manner that enables us to attract and retain outstanding director candidates and reflects the substantial time commitment necessary to oversee the Company's affairs. We also seek to align the interests of our directors and our stockholders and we have chosen to do so by compensating our non-employee directors with a mix of cash and equity-based compensation.

Cash Compensation

The fees that will be paid to our non-employee directors for service on the Board, and for service on each committee of the Board on which the director is then a member, and the fees that will be paid to the chairperson of the Board, if one is then appointed, and the chairperson of each committee of the Board will be as follows:

	Member Annual Fee	Chairman Incremental 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

The foregoing fees will be 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 the Board, on such committee or in such position.

Equity Compensation

Initial Grants . Upon initial election to the Board, each non-employee director will be granted, automatically and without the need for any further action by the Board, an initial equity award of an option to purchase 30,000 shares of our common stock. The initial award shall have a term of ten years from the date of the award, and shall vest and become exercisable as to 1/36 of the shares underlying such award at the end of each successive one-month period following the grant date until the third anniversary of the grant date, subject to the director's continued service to the Company through each applicable vesting date. The vesting shall accelerate as to 100% of the shares upon a change in control of the Company. The exercise price shall be the closing price of our common stock on the date of grant.

Annual Grants . Each non-employee director who has served as a member of the Board for at least six months prior to the date of our annual meeting of stockholders for a particular year will be granted, automatically and without the need for any further action by the Board, an equity award on the date of the first Board meeting held after our annual meeting of stockholders for such year of an option to purchase 15,000 shares of our common stock. The annual award shall have a term of ten years from the date of the award, and shall vest and become exercisable in full on the one-year 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 director's continued service to the Company through each applicable vesting date. The vesting shall accelerate as to 100% of the shares upon a change in control of the Company. The exercise price shall be the closing price of our common stock on the date of grant.

The foregoing share amounts shall be automatically adjusted 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 effecting our common stock, or any distribution to holders of our common stock other than an ordinary cash dividend.

The initial awards and the annual awards shall be subject to the terms and conditions of our 2019 Stock Incentive Plan, or any successor plan, and the terms of the option agreements entered into with each director in connection with such awards.

Expenses

Upon presentation of documentation of such expenses reasonably satisfactory to the Company, each non-employee director shall be reimbursed for his or her reasonable out-of-pocket business expenses incurred in connection with attending meetings of the Board and committees thereof or in connection with other business related to the Board, and each non-employee director shall also be reimbursed for his or her reasonable out-of-pocket business expenses authorized by the Board or a committee of the Board that are incurred in connection with attendance at various conferences or meetings with management of the Company, in accordance with the Company's travel policy, as it may be in effect from time to time.

EMPLOYMENT AGREEMENT

THIS EMPLOYMENT AGREEMENT (the “Agreement”), is made as of October 29, 2020 (the “Effective Date”) by and between Fulcrum Therapeutics, Inc. (the “Company”), and Curtis Oltmans (the “Executive”) (together, the “Parties”).

RECITALS

WHEREAS, the Company desires to continue to employ the Executive as its Senior Vice President, General Counsel; and

WHEREAS, the Company and the Executive are party to a letter agreement dated (the “Existing Agreement”) and desire to amend and restate the Existing Agreement in its entirety; and

WHEREAS, the Executive has agreed to accept such continued employment on the terms and conditions set forth in this Agreement;

NOW, THEREFORE, in consideration of the foregoing and of the respective covenants and agreements of the Parties herein contained, the Parties hereto agree as follows:

1. *Agreement.* This Agreement shall be effective as of the Effective Date. Following the Effective Date, the Executive shall continue to be an employee of the Company until such employment relationship is terminated in accordance with Section 7 hereof (the “Term of Employment”).
 2. *Position.* During the Term of Employment, the Executive shall serve as SVP, General Counsel of the Company, working out of the Company’s office in Cambridge, Massachusetts, and travelling as reasonably required by the Executive’s job duties.
 3. *Scope of Employment.* During the Term of Employment, the Executive shall be responsible for the performance of those duties consistent with the Executive’s position as SVP, General Counsel. The Executive shall report to the President and Chief Executive Officer of the Company and shall perform and discharge faithfully, diligently, and to the best of the Executive’s ability, the Executive’s duties and responsibilities hereunder. The Executive shall devote substantially all of the Executive’s business time, loyalty, attention and efforts to the business and affairs of the Company and its affiliates. Membership on boards of directors of any other companies will be permitted only with the express approval of the Company’s board of directors (the “Board”); provided, however, that the Executive may engage in community and charitable activities or participate in industry associations and serve on the boards of up to two (2) community, charitable or industry organizations, without the approval of the Board, provided such activities do not create a conflict of interest or otherwise interfere with the Executive’s performance of the Executive’s duties hereunder. The Executive agrees to abide by the rules, regulations, instructions, personnel practices and policies of the Company and any changes therein that may be adopted from time to time by the Company.
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4. *Compensation.* As full compensation for all services rendered by the Executive to the Company and any affiliate thereof, during the Term of Employment, the Company will provide to the Executive the following:

(a) *Base Salary.* The Executive shall receive a base salary at the annualized rate of \$390,000 (the "Base Salary"). The Executive's Base Salary shall be paid in equal installments in accordance with the Company's regularly established payroll procedures. The Executive's Base Salary will be reviewed on an annual or more frequent basis by the Board and is subject to change in the discretion of the Board.

(b) *Annual Discretionary Bonus.* The Executive will be eligible to earn an annual performance bonus of up to 35% of the Executive's Base Salary (the "Target Bonus"), based upon the Board's assessment of the Executive's performance and the Company's attainment of targeted goals as set by the Board in its sole discretion. To the extent the Executive's Base Salary and/or target bonus percentage of Base Salary is changed during the year to which the performance bonus relates, the Target Bonus shall be calculated based on base salary actually paid during such year (and not solely on the Executive's Base Salary at the end of such year) and shall apply the initial target bonus percentage of Base Salary and the revised target bonus percentage of Base Salary based on the portion of the year during which each was in effect. The Board may determine to provide the bonus in the form of cash, equity award(s), or a combination of cash and equity. Following the close of each calendar year, the Board will determine whether the Executive has earned a performance bonus, and the amount of any performance bonus, based on the set criteria. No amount of the annual bonus is guaranteed, and the Executive must be an employee in good standing on the date of payment in order to be eligible for any annual bonus, except as specifically set forth below. The annual performance bonus, if earned, will be paid by no later than March 15 of the calendar year after the year to which it relates. The Executive's bonus eligibility will be reviewed on an annual or more frequent basis by the Board and is subject to change in the discretion of the Board.

(c) *Equity Award.* The Executive will be eligible to receive equity awards, if any, at such times and on such terms and conditions as the Board shall, in its sole discretion, determine.

(d) *Paid Time Off.* The Executive shall be entitled to paid time off, vacation time plus sick time, consistent with the Company's policies.

(e) *Benefits.* Subject to eligibility requirements and the Company's policies, the Executive shall have the right, on the same basis as other similarly-situated employees of the Company, to participate in, and to receive benefits under, any medical, vision and dental insurance policy maintained by the Company and the Company shall pay a portion of the cost of the premiums for such medical, vision and dental insurance that is consistent with the Company's then current employee benefit policy if the Executive elects to participate in such plans.

(f) *Withholdings.* All compensation payable to the Executive shall be subject to applicable taxes and withholdings.

5. *Expenses.* The Executive will be reimbursed for her actual, necessary, and reasonable business expenses pursuant to Company policy, subject to the provisions of Section 3 of Exhibit A attached hereto.

6. *Restrictive Covenants Agreement.* The Executive hereby acknowledges the Employee Confidentiality and Assignment Agreement, dated October 27, 2020, that the Executive entered into with the Company.

7. *Employment Termination.* This Agreement and the employment of the Executive shall terminate upon the occurrence of any of the following:

(a) Upon the death or “Disability” of the Executive. As used in this Agreement, the term “Disability” shall mean a physical or mental illness or disability that prevents the Executive from performing the duties of the Executive’s position for a period of more than any three consecutive months or for periods aggregating more than twenty-six weeks. The Company shall determine in good faith and in its sole discretion whether the Executive is unable to perform the services provided for herein.

(b) At the election of the Company, with or without “Cause” (as defined below), immediately upon written notice by the Company to the Executive. As used in this Agreement, “Cause” shall mean:

- (i) Executive’s 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) Executive’s conviction of (A) a felony or (B) any misdemeanor involving moral turpitude, deceit, dishonesty or fraud;
- (iii) Executive’s 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, provided, however, that the Executive shall have a period of not less than ten (10) days to cure any curable act or omission constituting Cause described in this Section 7(b)(iii) following the Company’s delivery to the Executive of written notice of such act or omission; or
- (iv) Executive’s material violation of any provision of any agreement(s) between the Executive and the Company relating to nonsolicitation, nondisclosure and/or assignment of inventions.

(c) At the election of the Executive, with or without “Good Reason” (as defined below), immediately upon written notice by the Executive to the Company (subject, if it is with Good Reason, to the timing provisions set forth in the definition of Good Reason). As used in this Agreement, “Good Reason” shall mean (without the Executive’s consent):

- (i) a material diminution of the Executive's base compensation, other than in connection with, and substantially proportionate to, reductions by the Company of the base compensation of all or substantially all senior executives of the Company;
- (ii) a material diminution in the Executive's duties, authority or responsibilities;
- (iii) the Company's requiring Executive to relocate Executive's primary office more than fifty (50) miles from the Executive's then-current primary office; or
- (iv) any material breach of this Agreement or any other agreement between the Company and the Executive by the Company not otherwise covered by this paragraph;

provided, however, that in each case, the Company shall have a period of not less than thirty (30) days to cure any act constituting Good Reason following Executive's delivery to the Company of written notice within sixty (60) days of the action or omission constituting Good Reason and that the Executive actually terminates employment within thirty (30) days following the expiration of the Company's cure period.

8. *Effect of Termination.*

(a) *All Terminations Other Than by the Company Without Cause or by the Executive With Good Reason.* If the Executive's employment is terminated under any circumstances other than a Qualifying Termination (as defined below) (including a voluntary termination by the Executive without Good Reason pursuant to Section 7(c), a termination by the Company for Cause pursuant to Section 7(b) or due to the Executive's death or Disability pursuant to Section 7(a)), the Company's obligations under this Agreement shall immediately cease and the Executive shall only be entitled to receive (i) the Base Salary that has accrued and to which the Executive is entitled as of the effective date of such termination and to the extent consistent with general Company policy, to be paid in accordance with the Company's established payroll procedure and applicable law but no later than the next regularly scheduled pay period, (ii) unreimbursed business expenses for which the Executive has timely submitted appropriate documentation in accordance with Section 5 hereof, and (iii) any amounts or benefits to which the Executive is then entitled under the terms of the benefit plans then-sponsored by the Company in accordance with their terms (and not accelerated to the extent acceleration does not satisfy Section 409A of the Internal Revenue Code of 1986, as amended, (the "Code")) (the payments described in this sentence, the "Accrued Obligations").

(b) *Termination by the Company Without Cause or by the Executive With Good Reason Prior to or More Than Twelve Months Following a Change in Control.* If the Executive's employment is terminated by the Company without Cause pursuant to Section 7(b) or by the Executive with Good Reason pursuant to Section 7(c) (in either case, a "Qualifying Termination") prior to or more than twelve (12) months following a Change in Control (as defined below), the Executive shall be entitled to the Accrued Obligations. In addition, and subject to Exhibit A and the conditions of Section 8(d), the Company shall: (i) continue to pay to the Executive, in accordance with the Company's regularly established payroll procedures, the Executive's Base Salary for a

period of nine (9) months and (ii) provided the Executive is eligible for and timely elects to continue receiving group medical insurance pursuant to the “COBRA” law, continue to pay (but in no event longer than nine (9) months following the Executive’s termination date) the share of the premium for health coverage that is paid by the Company for active and similarly-situated employees who receive the same type of coverage, unless the Company’s provision of such COBRA payments will violate the nondiscrimination requirements of applicable law, in which case this benefit will not apply (collectively, the “Severance Benefits”).

(c) Termination by the Company Without Cause or by the Executive With Good Reason Within Twelve Months Following a *Change in Control*. If a Qualifying Termination occurs within twelve (12) months following a Change in Control, then the Executive shall be entitled to the Accrued Obligations. In addition, and subject to Exhibit A and the conditions of Section 8(d), the Company shall: (i) continue to pay to the Executive, in accordance with the Company’s regularly established payroll procedures, the Executive’s Base Salary (or, if higher, the Executive’s Base Salary in effect immediately prior to the Change in Control) for a period of twelve (12) months; (ii) pay to the Executive, in a single lump sum on the Payment Date (as defined below) an amount equal to 100% of the Executive’s Target Bonus for the year in which termination occurs or, if higher, the Executive’s Target Bonus immediately prior to the Change in Control, (iii) provided the Executive is eligible for and timely elects to continue receiving group medical insurance pursuant to the “COBRA” law, continue to pay (but in no event longer than twelve (12) months following the Executive’s termination date) the share of the premium for health coverage that is paid by the Company for active and similarly-situated employees who receive the same type of coverage, unless the Company’s provision of such COBRA payments will violate the nondiscrimination requirements of applicable law, in which case this benefit will not apply, and (iv) provide that the vesting of the Executive’s then-unvested equity awards that vest based solely on the passage of time shall be accelerated, such that all then-unvested equity awards that vest based solely on the passage of time vest and become fully exercisable or non- forfeitable as of the termination date (collectively, the “Change in Control Severance Benefits”).

(d) *Release*. As a condition of the Executive’s receipt of the Severance Benefits or the Change in Control Severance Benefits, as applicable, the Executive must execute and deliver to the Company a severance and release of claims agreement in a form to be provided by the Company (the “Severance Agreement”), which Severance Agreement must become irrevocable within 60 days following the date of the Executive’s termination of employment (or such shorter period as may be directed by the Company). The Severance Benefits or the Change in Control Severance Benefits, as applicable, will be paid or commence to be paid in the first regular payroll beginning after the Severance Agreement becomes effective, provided that if the foregoing 60 day period would end in a calendar year subsequent to the year in which the Executive’s employment ends, the Severance Benefits or Change in Control Severance Benefits, as applicable, will not be paid or begin to be paid before the first payroll of the subsequent calendar year (the date the Severance Benefits or Change in Control Severance Benefits, as applicable, commence pursuant to this sentence, the “Payment Date”). The Executive must continue to comply with the Employee Confidentiality and Assignment Agreement and any similar agreement with the Company in order to be eligible to continue receiving the Severance Benefits or Change in Control Severance Benefits, as applicable.

(e) *Change in Control Definition.* For purposes of this Agreement, “Change in Control” shall mean the occurrence of any of the following events, provided that such event or occurrence constitutes a change in the ownership or effective control of the Company, or a change in the ownership of a substantial portion of the assets of the Company, as defined in Treasury Regulation §§ 1.409A-3(i)(5)(v), (vi) and (vii): (i) the acquisition by an individual, entity or group (within the meaning of Section 13(d)(3) or 14(d)(2) of the Securities Exchange Act of 1934 (the “Exchange Act”)) (a “Person”) of beneficial ownership of any capital stock of the Company if, after such acquisition, such Person beneficially owns (within the meaning of Rule 13d-3 under the Exchange Act) fifty percent (50%) or more of either (x) the then-outstanding shares of common stock of the Company (the “Outstanding Company Common Stock”) or (y) the combined voting power of the then-outstanding securities of the Company entitled to vote generally in the election of directors (the “Outstanding Company Voting Securities”); provided, however, that for purposes of this subsection (i), the following acquisitions shall not constitute a Change in Control: (1) any acquisition directly from the Company or (2) any acquisition by any entity pursuant to a Business Combination (as defined below) which complies with clauses (x) and (y) of subsection (iii) of this definition; or (ii) a change in the composition of the Board that results in the Continuing Directors (as defined below) no longer constituting a majority of the Board (or, if applicable, the Board of Directors of a successor corporation to the Company), where the term “Continuing Director” means at any date a member of the Board (x) who was a member of the Board on the Effective Date or (y) who was nominated or elected subsequent to such date by at least a majority of the directors who were Continuing Directors at the time of such nomination or election or whose election to the Board was recommended or endorsed by at least a majority of the directors who were Continuing Directors at the time of such nomination or election; provided, however, that there shall be excluded from this clause (y) any individual whose initial assumption of office occurred as a result of an actual or threatened election contest with respect to the election or removal of directors or other actual or threatened solicitation of proxies or consents, by or on behalf of a person other than the Board; or (iii) the consummation of a merger, consolidation, reorganization, recapitalization or share exchange involving the Company, or a sale or other disposition of all or substantially all of the assets of the Company (a “Business Combination”), unless, immediately following such Business Combination, each of the following two (2) conditions is satisfied: (x) all or substantially all of the individuals and entities who were the beneficial owners of the Outstanding Company Common Stock and Outstanding Company Voting Securities immediately prior to such Business Combination beneficially own, directly or indirectly, more than fifty percent (50%) of the then-outstanding shares of common stock and the combined voting power of the then-outstanding securities entitled to vote generally in the election of directors, respectively, of the resulting or acquiring corporation in such Business Combination (which shall include, without limitation, a corporation which as a result of such transaction owns the Company or substantially all of the Company’s assets either directly or through one (1) or more subsidiaries) (such resulting or acquiring corporation is referred to herein as the “Acquiring Corporation”) in substantially the same proportions as their ownership of the Outstanding Company Common Stock and Outstanding Company Voting Securities, respectively, immediately prior to such Business Combination and (y) no Person (excluding any employee benefit plan (or related trust) maintained or sponsored by the Company or by the Acquiring Corporation) beneficially owns, directly or indirectly, fifty percent (50%) or more of the then-outstanding shares of common stock of the Acquiring Corporation, or of the combined voting power of the then-outstanding securities of such corporation entitled to vote generally in the election of

directors (except to the extent that such ownership existed prior to the Business Combination); or (iv) the liquidation or dissolution of the Company.

9. *Absence of Restrictions.* The Executive represents and warrants that the Executive is not bound by any employment contracts, restrictive covenants or other restrictions that prevent the Executive from entering into employment with, or carrying out the Executive's responsibilities for, the Company, or which are in any way inconsistent with any of the terms of this Agreement.

10. *Notice.* Any notice delivered under this Agreement shall be deemed duly delivered three (3) business days after it is sent by registered or certified mail, return receipt requested, postage prepaid, one (1) business day after it is sent for next-business day delivery via a reputable nationwide overnight courier service, or immediately upon hand delivery, in each case to the address of the recipient set forth below.

To Executive:

At the address set forth in the Executive's personnel file

To Company:

Fulcrum Therapeutics, Inc.
26 Landsdowne Street, 5th Floor
Cambridge, MA 02139

Either Party may change the address to which notices are to be delivered by giving notice of such change to the other Party in the manner set forth in this Section 10.

11. *Applicable Law; Jury Trial Waiver.* This Agreement shall be governed by and construed in accordance with the laws of the Commonwealth of Massachusetts (without reference to the conflict of laws provisions thereof). Any action, suit or other legal proceeding arising under or relating to any provision of this Agreement shall be commenced only in a court of the Commonwealth of Massachusetts (or, if appropriate, a federal court located within the Commonwealth of Massachusetts), and the Company and the Executive each consents to the jurisdiction of such a court. The Company and the Executive each hereby irrevocably waives any right to a trial by jury in any action, suit or other legal proceeding arising under or relating to any provision of this Agreement.

12. *Successors and Assigns.* This Agreement shall be binding upon and inure to the benefit of both Parties and their respective successors and assigns, including any corporation with which or into which the Company may be merged or which may succeed to its assets or business; provided, however, that the obligations of the Executive are personal and shall not be assigned by the Executive.

13. *At-Will Employment.* During the Term of Employment, the Executive will continue to be an at-will employee of the Company, which means that, notwithstanding any other provision set forth

herein, the employment relationship can be terminated by either Party for any reason, at any time, with or without prior notice and with or without Cause.

14. *Acknowledgment.* The Executive states and represents that the Executive has had an opportunity to fully discuss and review the terms of this Agreement with an attorney. The Executive further states and represents that the Executive has carefully read this Agreement, understands the contents herein, freely and voluntarily assents to all of the terms and conditions hereof, and signs the Executive's name of the Executive's own free act.

15. *No Oral Modification, Waiver, Cancellation or Discharge.* This Agreement may be amended or modified only by a written instrument executed by both the Company and the Executive. No delay or omission by the Company in exercising any right under this Agreement shall operate as a waiver of that or any other right. A waiver or consent given by the Company on any one occasion shall be effective only in that instance and shall not be construed as a bar to or waiver of any right on any other occasion.

16. *Captions and Pronouns.* The captions of the sections of this Agreement are for convenience of reference only and in no way define, limit or affect the scope or substance of any section of this Agreement. Whenever the context may require, any pronouns used in this Agreement shall include the corresponding masculine, feminine or neuter forms, and the singular forms of nouns and pronouns shall include the plural, and vice versa.

17. *Interpretation.* The Parties agree that this Agreement will be construed without regard to any presumption or rule requiring construction or interpretation against the drafting Party. References in this Agreement to "include" or "including" should be read as though they said "without limitation" or equivalent forms. References in this Agreement to the "Board" shall include any authorized committee thereof.

18. *Severability.* Each provision of this Agreement must be interpreted in such manner as to be effective and valid under applicable law, but if any provision of this Agreement is held to be prohibited by or invalid under applicable law, such provision will be ineffective only to the extent of such prohibition or invalidity, without invalidating the remainder of such provision or the remaining provisions of this Agreement. Moreover, if a court of competent jurisdiction determines any of the provisions contained in this Agreement to be unenforceable because the provision is excessively broad in scope, whether as to duration, activity, geographic application, subject or otherwise, it will be construed, by limiting or reducing it to the extent legally permitted, so as to be enforceable to the extent compatible with then applicable law to achieve the intent of the Parties.

19. *Entire Agreement.* This Agreement constitutes the entire agreement between the Parties and supersedes all prior agreements and understandings, whether written or oral, relating to the subject matter of this Agreement, including, without limitation, the Existing Agreement.

[Signatures on Page Following]

IN WITNESS WHEREOF, the Parties hereto have executed this Agreement as of the day and year set forth above.

FULCRUM THERAPEUTICS, INC.

By: /s/ Robert J. Gould

Name: Robert J. Gould

Title: President & Chief Executive Officer

EXECUTIVE:

/s/ Curtis Oltmans
Curtis Oltmans

EXHIBIT A

Payments Subject to Section 409A

1. Subject to this Exhibit A, any severance payments that may be due under the Agreement shall begin only upon the date of the Executive's "separation from service" (determined as set forth below) which occurs on or after the termination of the Executive's employment. The following rules shall apply with respect to distribution of the severance payments, if any, to be provided to the Executive under the Agreement, as applicable:

(a) It is intended that each installment of the severance payments provided under the Agreement shall be treated as a separate "payment" for purposes of Section 409A of the Internal Revenue Code ("Section 409A"). Neither the Company nor the Executive shall have the right to accelerate or defer the delivery of any such payments except to the extent specifically permitted or required by Section 409A.

(b) If, as of the date of the Executive's "separation from service" from the Company, the Executive is not a "specified employee" (within the meaning of Section 409A), then each installment of the severance payments shall be made on the dates and terms set forth in the letter agreement.

(c) If, as of the date of the Executive's "separation from service" from the Company, the Executive is a "specified employee" (within the meaning of Section 409A), then:

- (i) Each installment of the severance payments due under the Agreement that, in accordance with the dates and terms set forth herein, will in all circumstances, regardless of when the Executive's separation from service occurs, be paid within the short-term deferral period (as defined under Section 409A) shall be treated as a short-term deferral within the meaning of Treasury Regulation Section 1.409A-1(b)(4) to the maximum extent permissible under Section 409A and shall be paid on the dates and terms set forth in the Agreement; and
- (ii) Each installment of the severance payments due under the Agreement that is not described in this Exhibit A, Section 1(c)(i) and that would, absent this subsection, be paid within the six-month period following the Executive's "separation from service" from the Company shall not be paid until the date that is six months and one day after such separation from service (or, if earlier, the Executive's death), with any such installments that are required to be delayed being accumulated during the six-month period and paid in a lump sum on the date that is six months and one day following the Executive's separation from service and any subsequent installments, if any, being paid in accordance with the dates and terms set forth herein; provided, however, that the preceding provisions of this sentence shall not apply to any installment of payments if and to the maximum extent that that such

installment is deemed to be paid under a separation pay plan that does not provide for a deferral of compensation by reason of the application of Treasury Regulation 1.409A-1(b)(9)(iii) (relating to separation pay upon an involuntary separation from service). Any installments that qualify for the exception under Treasury Regulation Section 1.409A-1(b)(9)(iii) must be paid no later than the last day of the Executive's second taxable year following the taxable year in which the separation from service occurs.

2. The determination of whether and when the Executive's separation from service from the Company has occurred shall be made and in a manner consistent with, and based on the presumptions set forth in, Treasury Regulation Section 1.409A-1(h). Solely for purposes of Section 2 of this Exhibit A, "Company" shall include all persons with whom the Company would be considered a single employer under Section 414(b) and 414(c) of the Code.

3. All reimbursements and in-kind benefits provided under the Agreement shall be made or provided in accordance with the requirements of Section 409A to the extent that such reimbursements or in-kind benefits are subject to Section 409A, including, where applicable, the requirements that (i) any reimbursement is for expenses incurred during the Executive's lifetime (or during a shorter period of time specified in the Agreement), (ii) the amount of expenses eligible for reimbursement during a calendar year may not affect the expenses eligible for reimbursement in any other calendar year, (iii) the reimbursement of an eligible expense will be made on or before the last day of the calendar year following the year in which the expense is incurred and (iv) the right to reimbursement is not subject to set off or liquidation or exchange for any other benefit.

4. The Company makes no representation or warranty and shall have no liability to the Executive or to any other person if any of the provisions of the Agreement (including this Exhibit A) are determined to constitute deferred compensation subject to Section 409A but that do not satisfy an exemption from, or the conditions of, that section.

5. The Agreement is intended to comply with, or be exempt from, Section 409A and shall be interpreted accordingly.

[Remainder of page intentionally left blank.]

List of Subsidiaries

	Jurisdiction of Incorporation
Fulcrum Therapeutics Securities Corp.	Massachusetts

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

1. Registration Statement (Form S-8 No. 333-233452) pertaining to the 2016 Stock Incentive Plan, as amended, 2019 Stock Incentive Plan, and 2019 Employee Stock Purchase Plan of Fulcrum Therapeutics, Inc.,
2. Registration Statement (Form S-8 No. 333-236910) pertaining to the 2019 Stock Incentive Plan and 2019 Employee Stock Purchase Plan of Fulcrum Therapeutics, Inc.,
3. Registration Statement (Form S-1 No. 333-239353) and related Prospectus of Fulcrum Therapeutics, Inc.; and,
4. Registration Statement (Form S-3 No. 333-244136) and related Prospectus of Fulcrum Therapeutics, Inc.;

of our report dated March 4, 2021, with respect to the consolidated financial statements of Fulcrum Therapeutics, Inc. included in this Annual Report (Form 10-K) of Fulcrum Therapeutics, Inc. for the year ended December 31, 2020.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 4, 2021

**CERTIFICATION PURSUANT TO RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES
EXCHANGE ACT OF 1934, AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-
OXLEY ACT OF 2002**

I, Robert J. Gould, certify that:

1. I have reviewed this Annual Report on Form 10-K of Fulcrum Therapeutics, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:
 - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - (b) (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313);
 - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 4, 2021

By: /s/ Robert J. Gould
Robert J. Gould, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

**CERTIFICATION PURSUANT TO RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES
EXCHANGE ACT OF 1934, AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-
OXLEY ACT OF 2002**

I, Bryan Stuart, certify that:

1. I have reviewed this Annual Report on Form 10-K of Fulcrum Therapeutics, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:
 - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - (b) (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313);
 - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 4, 2021

By: /s/ Bryan Stuart

Bryan Stuart
Chief Operating Officer
(Principal Financial Officer)

**CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report on Form 10-K of Fulcrum Therapeutics, Inc. (the "Company") for the year ended December 31, 2020, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Robert J. Gould, President and Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to his knowledge:

- (1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 4, 2021

By: /s/ Robert J. Gould
Robert J. Gould, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

**CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report on Form 10-K of Fulcrum Therapeutics, Inc. (the “Company”) for the year ended December 31, 2020, as filed with the Securities and Exchange Commission on the date hereof (the “Report”), the undersigned, Bryan Stuart, Chief Operating Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to his knowledge:

- (1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 4, 2021

By: /s/ Bryan Stuart

Bryan Stuart
Chief Operating Officer
(Principal Financial Officer)