

The information in this preliminary prospectus supplement is not complete and may be changed. A registration statement has been filed with the Securities and Exchange Commission and is effective. This prospectus supplement is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Filed Pursuant to Rule 424(b)(5)
Registration No. 333-244136

SUBJECT TO COMPLETION, DATED JANUARY 19, 2021

PROSPECTUS SUPPLEMENT
(to Prospectus dated August 17, 2020)

Shares



Common Stock

We are offering _____ shares of our common stock in this offering.

Our common stock is listed on the Nasdaq Global Market under the symbol "FULC." The last reported sales price of our common stock on the Nasdaq Global Market on January 15, 2021 was \$11.00 per share.

	Per Share	Total
Public offering price	\$	\$
Underwriting discounts and commissions(1)	\$	\$
Proceeds to Fulcrum, before expenses	\$	\$

(1) We have agreed to reimburse the underwriters for certain FINRA-related expenses. See "Underwriting" for additional information regarding the compensation payable to the underwriters.

We have granted the underwriters an option for a period of 30 days to purchase up to an additional _____ shares of our common stock.

Investing in our common stock involves risks. See "[Risk Factors](#)" beginning on page S-7 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement.

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

The underwriters expect to deliver the shares of common stock to purchasers on or about _____, 2021.

Joint Bookrunning Managers

SVB Leerink

Piper Sandler

Credit Suisse

The date of this prospectus supplement is _____, 2021.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this common stock offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference herein. The second part, the accompanying prospectus, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement and the information contained in the accompanying prospectus or any document incorporated by reference therein filed prior to the date of this prospectus supplement, you should rely on the information in this prospectus supplement; provided that if any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference in the accompanying prospectus—the statement in the document having the later date modifies or supersedes the earlier statement.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference herein were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

Neither we nor the underwriters have authorized anyone to provide any information other than that contained or incorporated by reference into this prospectus supplement, the accompanying prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We and the underwriters take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus supplement and the accompanying prospectus do not constitute an offer to sell, or a solicitation of an offer to purchase, the securities offered by this prospectus supplement and the accompanying prospectus in any jurisdiction to or from any person to whom or from whom it is unlawful to make such offer or solicitation of an offer in such jurisdiction. The information contained in this prospectus supplement or the accompanying prospectus, or incorporated by reference herein or therein is accurate only as of the respective dates thereof, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or of any sale of our common stock. It is important for you to read and consider all information contained in this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein and therein, in making your investment decision. You should also read and consider the information in the documents to which we have referred you in the sections entitled “Where You Can Find More Information” and “Incorporation of Certain Information By Reference” in this prospectus supplement and in the accompanying prospectus.

We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the accompanying prospectus and the offering of the common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus supplement and the accompanying prospectus outside the United States. This prospectus supplement and the accompanying prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

Unless the context otherwise indicates, references in this prospectus to “we,” “our” and “us” refer, collectively, to Fulcrum Therapeutics, Inc., a Delaware corporation, and its consolidated subsidiary.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information contained elsewhere in this prospectus supplement and the accompanying prospectus and in the documents we incorporate by reference herein and therein. This summary does not contain all of the information you should consider before investing in our common stock. You should read this entire prospectus supplement and accompanying prospectus carefully, especially the risks of investing in our common stock discussed under "Risk Factors" beginning on page S-7 of this prospectus supplement and in our Annual Report on Form 10-K for the year ended December 31, 2019 and our Quarterly Report on Form 10-Q for the period ended September 30, 2020, along with our consolidated financial statements and notes to those consolidated financial statements and the other information incorporated by reference into this prospectus supplement and the accompanying prospectus, before making an investment decision.

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

ReDUX4 is a randomized, double-blind, placebo-controlled multicenter international Phase 2b clinical trial in 80 subjects with FSHD to investigate the efficacy and safety of oral administration of losmapimod 15 mg twice per day. The primary endpoint is to evaluate the reduction of DUX4-driven gene expression in affected skeletal muscle biopsies. 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 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 have 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 68 subjects who did not complete the original 24-week treatment period remain active 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.

In June 2020, we announced plans to evaluate losmapimod as a potential treatment for patients with COVID-19. On June 24, 2020, we announced that we received notification from the U.S. Food and Drug Administration, or 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. We intend to conduct an interim analysis for futility and sample size re-estimation using an independent data monitoring committee when approximately 50 percent of subjects complete the 28-day visit. We expect to provide an update regarding the timing of the LOSVID trial by the end of the first quarter of 2021.

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 will be a randomized, double-blind, placebo-controlled, single ascending dose (SAD) study in up to six cohorts. Part B will be a randomized, double-blind, placebo-controlled, multiple ascending dose (MAD) study in up to four cohorts dosed once daily for 14 days. Part C will be an open label pilot food effect study in subjects randomized to take FTX-6058 with and without a high-fat meal, and Part D will be 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.

Recent Developments

Although we have not finalized our full financial results for the fourth quarter and fiscal year ended December 31, 2020, we expect to report that we had cash, cash equivalents and marketable securities of approximately \$112.9 million as of December 31, 2020.

The estimated cash figure is preliminary and unaudited, represents a management estimate as of the date of this prospectus supplement and is subject to completion of our financial closing procedures. Our independent

registered public accounting firm has not conducted an audit or review of, and does not express an opinion or any other form of assurance with respect to, the estimated cash figure.

From October 1, 2020 through December 31, 2020, we sold 550,000 shares of our common stock in an at-the-market offering for aggregate net proceeds of \$5.7 million.

On January 15, 2021, Owen Wallace, our chief scientific officer, notified us of his intent to resign to pursue a new career opportunity. Dr. Wallace is expected to continue in his current role until February 5, 2021. Following his resignation, Dr. Wallace will join our scientific advisory board. We expect Christopher Moxham to serve as chief scientific officer following the effective date of Dr. Wallace's resignation. Dr. Moxham currently serves as our senior vice president of discovery.

Risks Associated with Our Business

Our business is subject to a number of risks of which you should be aware before making an investment decision. These risks are discussed more fully in the "Risk Factors" section of this prospectus supplement immediately following this prospectus supplement summary, in our Annual Report on Form 10-K for the year ended December 31, 2019 and in our Quarterly Report on Form 10-Q for the period ended September 30, 2020, which are incorporated by reference herein. These risks include, but are not limited to, the following:

- We have incurred significant losses since our inception. We expect to incur losses over the next several years and may never achieve or maintain profitability. As of September 30, 2020, we had an accumulated deficit of \$203.9 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.
- 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 develop losmapimod for the treatment of patients with COVID-19.
- We may not be successful in our efforts to use our product engine to build a pipeline of product candidates.
- Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. The results of preclinical studies and early clinical trials may not be predictive of future results. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.
- Because we are developing some of our product candidates for the treatment of diseases in which there is little clinical experience and, in some cases, using new endpoints or methodologies, such as the measurement of DUX4-driven gene expression in muscle biopsies in our Phase 2b clinical trial of losmapimod for the treatment of FSHD, the FDA or other regulatory authorities may not consider the endpoints of our clinical trials to predict or provide clinically meaningful results.
- If serious adverse events or unacceptable side effects are identified during the development of our product candidates, we may need to abandon or limit our development of some of our product candidates.

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

Our Corporate Information

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

We own or have rights, or have applied for, to trademarks, service marks and trade names that we use in connection with the operation of our business, including our corporate name, logos and website names. Other trademarks, service marks and trade names appearing in this prospectus are the property of their respective owners. Solely for convenience, some of the trademarks, service marks and trade names referred to in this prospectus are listed without the ® and ™ symbols, but we will assert, to the fullest extent under applicable law, our rights to our trademarks, service marks and trade names.

Implications of Being an Emerging Growth Company and a Smaller Reporting Company

As a company with less than \$1.07 billion in revenue during our last fiscal year, we qualify as an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and we may remain an emerging growth company until December 31, 2024 or until such earlier time as we have more than \$1.07 billion in annual revenue, the market value of our stock held by non-affiliates is more than \$700 million as of our most recently completed second fiscal quarter or we issue more than \$1 billion of non-convertible debt over a three-year period. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure and other requirements that are applicable to public companies that are not emerging growth companies.

We are also a “smaller reporting company,” meaning that the market value of our stock held by non-affiliates is less than \$700 million as of our most recently completed second fiscal quarter and our annual revenue was less than \$100 million during our most recently completed fiscal year. We may continue to be a smaller reporting company if either (i) the market value of our stock held by non-affiliates is less than \$250 million or (ii) our

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annual revenue was less than \$100 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than \$700 million as of our most recently completed second fiscal quarter. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies.

THE OFFERING

Common Stock Offered	shares.
Common Stock to be Outstanding Immediately Following this Offering	shares.
Option to Purchase Additional Shares	We have granted the underwriters an option for a period of 30 days to purchase from us up to an additional shares of our common stock.
Use of Proceeds	<p>We estimate that the net proceeds to us from this offering will be approximately \$ million, or approximately \$ million if the underwriters exercise their option to purchase additional shares in full, in each case after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.</p> <p>We intend to use the net proceeds from this offering, together with our existing cash, cash equivalents and marketable securities, to advance losmapimod for FSHD and COVID-19, to advance FTX-6058 for certain hemoglobinopathies, to fund our ongoing product engine and discovery efforts and for working capital and other general corporate purposes. See “Use of Proceeds.”</p>
Risk Factors	You should read the “Risk Factors” section of this prospectus supplement beginning on page S-7 and in our Annual Report on Form 10-K for the year ended December 31, 2019 and our Quarterly Report on Form 10-Q for the period ended September 30, 2020 for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.
Nasdaq Global Market Symbol	“FULC”

The number of shares of our common stock to be outstanding immediately after this offering is based on 28,067,434 shares of our common stock outstanding as of January 8, 2021, including 115,646 shares of unvested restricted stock subject to repurchase by us. The number of shares of our common stock to be outstanding after this offering excludes:

- 2,962,315 shares of common stock issuable upon exercise of stock options outstanding as of January 8, 2021, at a weighted average exercise price of \$11.57 per share; and
- 2,851,312 and 746,673 shares of common stock reserved for future issuance under our 2019 Stock Incentive Plan and our 2019 Employee Stock Purchase Plan, respectively, as of January 8, 2021.

Unless otherwise indicated, all information in this prospectus supplement:

- assumes no exercise of the outstanding stock options described above;
- assumes no exercise by the underwriters of their option to purchase additional shares of our common stock; and
- does not reflect the potential issuance of shares of our common stock that remain available for sale as of the date of this prospectus supplement under our “at-the-market” offering program, pursuant to which we may sell common stock for remaining gross proceeds of up to \$69.1 million from time to time under our equity distribution agreement with Piper Sandler & Co.

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before you decide to invest in our common stock, you should carefully consider the risks and uncertainties described below and in our Annual Report on Form 10-K for the year ended December 31, 2019 and our Quarterly Report on Form 10-Q for the period ended September 30, 2020, together with all other information contained in this prospectus supplement, the accompanying prospectus and in our filings with the Securities and Exchange Commission, or SEC, that we have incorporated by reference into this prospectus supplement and the accompanying prospectus. If any of the following risks actually occurs, our business, prospects, operating results and financial condition could suffer materially. In such event, the trading price of our common stock could decline and you might lose all or part of your investment.

Risks Related to Our Common Stock and This Offering

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

The price of our common stock to be sold in this offering is substantially higher than the net tangible book value per share of our common stock. Therefore, if you purchase shares of our common stock in this offering, you will pay a price per share that substantially exceeds our net tangible book value per share after this offering. Based on the public offering price of \$ _____ per share, you will experience immediate dilution of \$ _____ per share, representing the difference between our as adjusted net tangible book value per share after giving effect to the sale by us of _____ shares in this offering at the public offering price. For additional information on the dilution that you will experience immediately after this offering, see the section titled “Dilution” in this prospectus supplement.

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. During the period from July 18, 2019 to January 15, 2021, the closing price of our common stock ranged from a high of \$22.06 per share to a low of \$4.46 per share. 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.

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

Although we currently intend to use the net proceeds from this offering, together with our existing cash, cash equivalents and marketable securities, in the manner described in the section titled “Use of Proceeds” in this prospectus supplement, our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

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

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

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein contain forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended, that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management and expected market growth are forward-looking statements. The words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein include, among other things, statements about:

- 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, and our ongoing Phase 3 clinical trial for the treatment of the novel coronavirus, or COVID-19;
- our ongoing Phase 1 clinical trial of FTX-6058 and our planned clinical trial of FTX-6058 in patients with 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 and any other product candidates, including in combination with other drugs and therapies;
- the timing of and our ability to submit applications for, obtain and maintain regulatory approvals for losmapimod and other product candidates;
- our expectations regarding our ability to fund our operating expenses and capital expenditure requirements with our cash, cash equivalents, and marketable securities and proceeds of this offering;
- the potential advantages of our product candidates;
- the rate and degree of market acceptance and clinical utility of our products;
- our estimates regarding the potential market opportunity for our product candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position;
- the progress and results of our collaborations with Acceleron Pharma Inc. and MyoKardia, Inc.;
- our ability to identify additional products, product candidates or technologies with significant commercial potential that are consistent with our commercial objectives;
- our expectations related to the use of proceeds from this offering;
- our estimates regarding expenses, future revenue, timing of any future revenue, capital requirements and needs for additional financing;
- the impact of government laws and regulations;
- our competitive position;

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- 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 prospectus supplement, particularly in the “Risk Factors” section in this prospectus supplement and in our Annual Report on Form 10-K for the year ended December 31, 2019 and our Quarterly Report on Form 10-Q for the period ended September 30, 2020, which are incorporated by reference herein, that 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 that we may make or enter into.

You should read this prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein completely and with the understanding that our actual future results may be materially different from what we expect. 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 law.

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

USE OF PROCEEDS

We estimate that the net proceeds to us from the issuance and sale of _____ shares of common stock in this offering will be approximately \$ _____ million, or approximately \$ _____ million if the underwriters exercise their option to purchase additional shares in full, in each case after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

We expect to use the net proceeds from this offering, together with our existing cash, cash equivalents and marketable securities, to advance losmapimod for FSHD and COVID-19, to advance FTX-6058 for certain hemoglobinopathies, to fund our ongoing product engine and discovery efforts and for working capital and other general corporate purposes.

As of September 30, 2020, we had cash, cash equivalents and marketable securities of \$127.0 million. From October through December 2020, we sold 550,000 shares of our common stock in an at-the-market offering for aggregate net proceeds of \$5.7 million.

We believe that the net proceeds from this offering, together with our existing cash, cash equivalents and marketable securities will enable us to fund our operating expenses and capital expenditure requirements into _____. We have based this estimate on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect.

We will require additional capital to complete clinical development of each of our product candidates and to commercialize any of our product candidates, if we receive regulatory approval.

This expected use of net proceeds from this offering and our existing cash, cash equivalents and marketable securities represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development, the status of and results from clinical trials, the timing of regulatory submissions and the outcome of regulatory review, as well as any collaborations that we may enter into with third parties for our product candidates, and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering. We have no current agreements, commitments or understandings for any material acquisitions or licenses of any products, businesses or technologies.

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

DIVIDEND POLICY

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

DILUTION

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

Our historical net tangible book value as of September 30, 2020 was \$105.0 million, or \$3.82 per share of common stock. Our historical net tangible book value is the amount of our total tangible assets less our total liabilities. Historical net tangible book value per share represents our historical net tangible book value divided by the 27,459,196 shares of common stock outstanding as of September 30, 2020, including 181,213 shares of unvested restricted stock subject to repurchase by us.

After giving effect to the issuance and sale of _____ shares of common stock that we are offering at the public offering price of \$ _____ per share, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2020 would have been \$ _____ million, or \$ _____ per share. This represents an immediate increase of \$ _____ in as adjusted net tangible book value per share to existing stockholders and immediate dilution of \$ _____ in as adjusted net tangible book value per share to investors purchasing shares of our common stock in this offering. Dilution per share to new investors is determined by subtracting as adjusted net tangible book value per share after this offering from the public offering price per share paid by new investors. The following table illustrates this dilution:

Public offering price per share	\$
Historical net tangible book value per share as of September 30, 2020	\$3.82
Increase in as adjusted net tangible book value per share attributable to new investors purchasing shares of common stock in this offering	<u> </u>
As adjusted net tangible book value per share immediately after this offering	<u> </u>
Dilution per share to new investors purchasing shares of common stock in this offering	<u><u> </u></u>

If the underwriters exercise their option to purchase additional shares in full the immediate dilution in as adjusted net tangible book value per share to investors in this offering would be \$ _____ per share.

The table and discussion above are based on the number of shares of our common stock outstanding as of September 30, 2020, including 181,213 shares of unvested restricted stock subject to repurchase by us, and exclude:

- 2,868,693 shares of common stock issuable upon exercise of stock options outstanding as of September 30, 2020, at a weighted average exercise price of \$11.62 per share;
- an additional 319,800 shares of common stock issuable upon exercise of stock options granted after September 30, 2020 at a weighted average exercise price of \$10.94 per share;
- 1,860,978 and 485,497 shares of common stock reserved for future issuance as of September 30, 2020 under our 2019 Stock Incentive Plan and our 2019 Employee Stock Purchase Plan, respectively; and
- 550,000 shares of common stock issued and sold after September 30, 2020 pursuant to our “at-the-market” offering program for aggregate gross sale proceeds of \$5.9 million, before deducting sales commissions and offering expenses, and the potential issuance of shares of common stock that

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remain available for sale as of the date of this prospectus supplement under our “at-the-market” offering program, pursuant to which we may sell common stock for remaining gross proceeds of up to \$69.1 million from time to time under our equity distribution agreement with Piper Sandler & Co.

To the extent that outstanding stock options are exercised, new stock options are issued, or we issue additional shares of common stock in the future, including pursuant to our equity distribution agreement with Piper Sandler & Co., there will be further dilution to investors purchasing shares of common stock in this offering.

The as adjusted information discussed above will be based on the actual number of shares, the offering price and other terms determined at pricing of this offering.

MATERIAL U.S. FEDERAL INCOME AND ESTATE TAX CONSIDERATIONS FOR NON-U.S. HOLDERS OF COMMON STOCK

The following is a discussion of material U.S. federal income and estate tax considerations relating to the ownership and disposition of shares of our common stock acquired in this offering by a non-U.S. holder. For purposes of this discussion, the term “non-U.S. holder” means a beneficial owner (other than a partnership or other pass-through entity) of our common stock that is not, for U.S. federal income tax purposes:

- an individual who is a citizen or resident of the United States;
- a corporation, or other entity treated as a corporation for U.S. federal income tax purposes, created or organized in or under the laws of the United States or of any political subdivision of the United States;
- an estate the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust if (1) a U.S. court is able to exercise primary supervision over the administration of the trust and one or more U.S. persons has authority to control all substantial decisions of the trust or (2) the trust has a valid election in effect under applicable U.S. Treasury Regulations to be treated as a U.S. person.

This discussion does not address the tax treatment of partnerships or other entities that are pass-through entities for U.S. federal income tax purposes or persons who hold shares of our common stock through partnerships or such other pass-through entities. The tax treatment of a partner in a partnership or other entity that is treated as a pass-through entity for U.S. federal income tax purposes generally will depend upon the status of the partner and the activities of the partnership. A partner in a partnership or other pass-through entity that will hold our common stock should consult his, her or its own tax advisor regarding the tax consequences of the purchase, ownership and disposition of our common stock through a partnership or other pass-through entity, as applicable.

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, which we refer to as the Code, existing and proposed U.S. Treasury Regulations promulgated thereunder, current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus supplement and all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any change or differing interpretation could alter the tax consequences to non-U.S. holders described in this prospectus supplement. There can be no assurance that the Internal Revenue Service, or the IRS, will not challenge one or more of the tax consequences described in this prospectus supplement.

This discussion addresses only non-U.S. holders that hold shares of our common stock as a capital asset (generally, property held for investment) for U.S. federal income tax purposes. This discussion does not address all aspects of U.S. federal income and estate taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder’s individual circumstances nor does it address any aspects of U.S. state, local or non-U.S. taxes, the alternative minimum tax, or the Medicare tax on net investment income. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as:

- financial institutions;
- brokers or dealers in securities;
- tax-exempt or governmental organizations;
- pension plans;
- owners that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment or who have elected to mark securities to market;
- insurance companies;
- controlled foreign corporations;

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- non-U.S. governments;
- passive foreign investment companies; and
- certain U.S. expatriates.

THIS DISCUSSION IS FOR INFORMATION ONLY AND IS NOT, AND IS NOT INTENDED TO BE, LEGAL OR TAX ADVICE. PROSPECTIVE INVESTORS SHOULD CONSULT THEIR OWN TAX ADVISORS REGARDING THE U.S. FEDERAL, STATE, LOCAL, ESTATE AND NON-U.S. INCOME AND OTHER TAX CONSIDERATIONS OF ACQUIRING, HOLDING AND DISPOSING OF OUR COMMON STOCK, INCLUDING THE CONSEQUENCES OF ANY PROPOSED CHANGES IN APPLICABLE LAWS.

Distributions

As discussed under the heading “Dividend Policy” above, we do not expect to pay cash dividends to holders of our common stock in the foreseeable future. If we make distributions in respect of our common stock, those distributions generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder’s investment, up to the non-U.S. holder’s tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below under the heading “Gain on Sale, Exchange or Other Taxable Disposition of Our Common Stock.” Any such distributions will also be subject to the discussions below under the headings “Information Reporting and Backup Withholding” and “FATCA.”

Dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder’s country of residence.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States, and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements (generally including provision of a properly executed IRS Form W-8ECI (or applicable successor form) certifying that the dividends are effectively connected with the non-U.S. holder’s conduct of a trade or business within the United States). However, such U.S. effectively connected income is taxed on a net income basis at the same U.S. federal income tax rates applicable to U.S. persons (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is classified as a corporation for U.S. federal income tax purposes may also, under certain circumstances, be subject to an additional “branch profits tax” at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder’s country of residence.

A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder’s country of residence generally will be required to provide a properly executed IRS Form W-8BEN or W-8BEN-E (or successor form) and satisfy applicable certification and other requirements.

Non-U.S. holders are urged to consult their own tax advisors regarding their entitlement to benefits under a relevant income tax treaty and the specific methods available to them to satisfy these requirements.

A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim with the IRS.

Gain on Sale, Exchange or Other Taxable Disposition of Our Common Stock

Subject to the discussion below under the headings “Information Reporting and Backup Withholding” and “FATCA,” a non-U.S. holder generally will not be subject to U.S. federal income tax or withholding tax on any gain realized upon such non-U.S. holder’s sale, exchange or other disposition of our common stock unless:

- the gain is effectively connected with the non-U.S. holder’s conduct of a trade or business in the United States, and, if an applicable income tax treaty so provides, the gain is attributable to a permanent establishment or fixed base maintained by the non-U.S. holder in the United States, in which case, the non-U.S. holder generally will be taxed on a net income basis at the U.S. federal income tax rates applicable to U.S. persons with respect to the gain, and, if the non-U.S. holder is a foreign corporation, an additional branch profits tax at a rate of 30% (or a lower rate as may be specified by an applicable income tax treaty between the United States and such holder’s country of residence) may also apply;
- the non-U.S. holder is a non-resident alien present in the United States for 183 days or more in the taxable year of the disposition and certain other requirements are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder’s country of residence) on the net gain derived from the disposition, which may be offset by certain U.S.-source capital losses of the non-U.S. holder, if any; or
- we are, or have been, at any time during the five-year period preceding such disposition (or the non-U.S. holder’s holding period, if shorter) a “U.S. real property holding corporation,” unless our common stock is regularly traded on an established securities market and the non-U.S. holder held no more than 5% of our outstanding common stock, directly or indirectly, during the shorter of the five-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. If we are determined to be a “U.S. real property holding corporation” and the foregoing exception does not apply, then the non-U.S. holder generally will be taxed on its net gain derived from the disposition at the U.S. federal income tax rates applicable to U.S. persons. Generally, a corporation is a “U.S. real property holding corporation” only if the fair market value of its “U.S. real property interests” (as defined in the Code and applicable Treasury Regulations) equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we do not believe that we are, or have been, a “U.S. real property holding corporation” for U.S. federal income tax purposes, or that we are likely to become one in the future. No assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rule described above.

U.S. Federal Estate Tax

Shares of our common stock that are owned or treated as owned by an individual who is a non-U.S. holder (as specially defined for U.S. federal estate tax purposes) at the time of death are considered U.S.-situs assets and will be included in the individual’s gross estate for U.S. federal estate tax purposes. Such shares, therefore, may be subject to U.S. federal estate tax, unless an applicable estate tax or other treaty provides otherwise.

Information Reporting and Backup Withholding

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock paid to such holder and the tax withheld, if any, with respect to such distributions. Non-U.S. holders generally will have to comply with specific certification procedures to establish that the holder is not a U.S. person (as defined in the Code) in order to avoid backup withholding at the applicable rate with respect to dividends on our common stock. Generally, a non-U.S. holder will comply with such procedures if it provides a properly executed IRS Form W-8BEN or W-8BEN-E (or other applicable IRS Form W-8), or otherwise meets documentary evidence requirements for establishing that it is a non-U.S. holder, or otherwise establishes an exemption. Dividends paid to non-U.S. holders subject to withholding of U.S. federal income tax, as described above under the heading “—Distributions,” will generally be exempt from U.S. backup withholding.

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Information reporting and backup withholding generally will apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or non-U.S., unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Non-U.S. holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that an appropriate claim is timely filed with the IRS.

FATCA

Provisions of the Code commonly referred to as the Foreign Account Tax Compliance Act, or FATCA, generally impose a 30% withholding tax on dividends on, and gross proceeds from the sale or other disposition of, our common stock if paid to a foreign entity unless (i) if the foreign entity is a "foreign financial institution," the foreign entity undertakes certain due diligence, reporting, withholding and certification obligations, (ii) if the foreign entity is not a "foreign financial institution," the foreign entity identifies certain of its U.S. investors, if any, or (iii) the foreign entity is otherwise exempt under FATCA.

Withholding under FATCA generally applies to payments of dividends on our common stock. While withholding under FATCA may also apply to payments of gross proceeds from a sale or other disposition of our common stock, under proposed U.S. Treasury Regulations, withholding on payments of gross proceeds is not required. Although such proposed regulations are not final, applicable withholding agents may rely on the proposed regulations until final regulations are issued.

If withholding under FATCA is required on any payment related to our common stock, investors not otherwise subject to withholding (or that otherwise would be entitled to a reduced rate of withholding) on such payment may be required to seek a refund or credit from the IRS. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this section. Non-U.S. holders should consult their own tax advisors regarding the possible implications of FATCA on their investment in our common stock and the entities through which they hold our common stock.

The preceding discussion of material U.S. federal tax considerations is for information only. It is not, and is not intended to be, legal or tax advice. Prospective investors should consult their own tax advisors regarding the particular U.S. federal, state, local, estate and non-U.S. income and other tax consequences of acquiring, holding and disposing of our common stock, including the consequences of any proposed changes in applicable laws.

UNDERWRITING

SVB Leerink LLC, Piper Sandler & Co. and Credit Suisse Securities (USA) LLC are acting as the representatives of each of the underwriters named below and as joint bookrunning managers for this offering. Subject to the terms and conditions set forth in the underwriting agreement among us and the underwriters, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the number of shares of common stock set forth opposite its name below.

<u>Underwriter</u>	<u>Number of Shares</u>
SVB Leerink LLC	
Piper Sandler & Co.	
Credit Suisse Securities (USA) LLC.	
Total	

Subject to the terms and conditions set forth in the underwriting agreement, the underwriters have agreed, severally and not jointly, to purchase all of the shares sold under the underwriting agreement if any of the shares are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make in respect of those liabilities.

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, including the validity of the shares, and subject to other conditions contained in the underwriting agreement, such as the receipt by the underwriters of officers' certificates and legal opinions. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Discounts and Commissions

The representatives have advised us that the underwriters propose initially to offer the shares to the public at the public offering price set forth on the cover page of this prospectus supplement and to dealers at that price less a concession not in excess of \$ per share. After the initial offering of the shares, the public offering price, concession or any other term of this offering may be changed by the representatives.

The following table shows the public offering price, underwriting discounts and commissions and proceeds, before expenses, to us. The information assumes either no exercise or full exercise by the underwriters of their option to purchase additional shares of our common stock.

	<u>Per Share</u>	<u>Total</u>	
		<u>Without Option</u>	<u>With Option</u>
Public offering price	\$	\$	\$
Underwriting discounts and commissions	\$	\$	\$
Proceeds, before expenses, to us	\$	\$	\$

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately \$. We also have agreed to reimburse the underwriters for up to \$10,000 for their FINRA counsel fee. In accordance with FINRA Rule 5110, this reimbursed fee is deemed underwriting compensation for this offering.

Option to Purchase Additional Shares

We have granted an option to the underwriters, exercisable for 30 days after the date of this prospectus supplement, to purchase up to additional shares at the public offering price, less underwriting discounts and commissions. If the underwriters exercise this option, each underwriter will be obligated, subject to the conditions contained in the underwriting agreement, to purchase a number of additional shares proportionate to that underwriter's initial amount reflected in the above table.

No Sales of Similar Securities

We, our executive officers and directors and certain of our other existing security holders have agreed not to sell or transfer any common stock or securities convertible into or exchangeable or exercisable for common stock, for 90 days after the date of this prospectus supplement without first obtaining the written consent of SVB Leerink LLC and Piper Sandler & Co. on behalf of the underwriters. Specifically, we and these other persons have agreed, with certain limited exceptions, not to directly or indirectly:

- offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of, directly or indirectly, any shares of common stock or any securities convertible into or exercisable or exchangeable for shares of common stock, or make any public announcement of an intention to do any of the foregoing;
- file, or demand filing of, any registration statement with the SEC relating to the offering of any shares of common stock or any securities convertible into or exercisable or exchangeable for common stock; or
- enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the common stock,

whether any such transaction described above is to be settled by delivery of common stock or such other securities, in cash or otherwise. In addition, we and each such person agrees that, without the prior written consent of the underwriters, we or such other person will not, during the restricted period, make any demand for, or exercise any right with respect to, the registration of any shares of common stock or any security convertible into or exercisable or exchangeable for common stock.

The restrictions on transfers or other dispositions by holders of our outstanding securities described in the immediately preceding paragraph do not apply to:

- transactions relating to shares of common stock or other securities acquired in this offering or in open market transactions after the completion of this offering, provided that no filing under Section 16(a) of the Exchange Act shall be required or shall be voluntarily made in connection with subsequent sales of common stock or other securities acquired in such open market transactions;
- transfers of shares of common stock or any security convertible into or exercisable or exchangeable for common stock as a bona fide gift or gifts, or to a charitable organization or educational institution in a transaction not involving a disposition for value;
- transfers of shares of common stock or any security convertible into or exercisable or exchangeable for common stock to any member of the immediate family of the signatory or any trust for the direct or indirect benefit of the signatory or the immediate family of the signatory in a transaction not involving a disposition for value;
- transfers of shares of common stock or any security convertible into or exercisable or exchangeable for common stock (i) by will, other testamentary document or intestate succession to the legal representative, heir, beneficiary or a member of the immediate family of the signatory upon the death of the signatory or (ii) solely by operation of law pursuant to a qualified domestic order or in connection with a divorce settlement;

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- if the signatory is an entity, transfers or distributions of shares of common stock or any security convertible into common stock to general or limited partners, members or stockholders of the signatory, the signatory's direct and indirect affiliates, or to an investment fund or other entity that controls or manages, or is under common control with, the signatory;
- transfers or dispositions of shares of common stock or any security convertible into or exercisable or exchangeable for common stock to us pursuant to any contractual arrangement in effect on the date of the lock-up agreement and disclosed to the underwriters that provides for the repurchase of the signatory's common stock or other securities by us or in connection with the termination of the signatory's employment with or service to us; provided that, subject to certain limited exceptions, no filing under Section 16(a) of the Exchange Act reporting a reduction in beneficial ownership of shares of common stock shall be required or shall be voluntarily made during the restricted period in connection with any such transfers or dispositions;
- the exercise of stock options to purchase shares of common stock granted under plans described in this prospectus and any related transfer to us of shares of common stock, subject to certain limitations, including that any shares of common stock received upon exercise shall be subject to the restrictions on transfer set forth in the lock-up agreement; provided that, subject to certain limited exceptions, no filing under Section 16(a) of the Exchange Act reporting a reduction in beneficial ownership of shares of common stock shall be required or shall be voluntarily made during the restricted period;
- the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of shares of common stock, provided that (i) such plan does not provide for the transfer of common stock during the restricted period and (ii) to the extent a public announcement or filing under the Exchange Act, if any, is required of or voluntarily made regarding the establishment of such plan, such announcement or filing shall include a statement to the effect that no transfer of common stock may be made under such plan during the restricted period;
- transfers of shares of common stock pursuant to a trading plan established pursuant to Rule 10b5-1 under the Exchange Act prior to the date hereof, which trading plan shall not be amended during the restricted period but may be terminated during the restricted period; or
- (i) transfers of shares of common stock (or any securities convertible into or exercisable or exchangeable for common stock) pursuant to a bona fide third-party tender offer for shares of our capital stock made to all holders of securities, merger, consolidation or other similar transaction approved by our board of directors the result of which is a change of control or (ii) entry into any lock-up, voting or similar agreement pursuant to which the signatory may agree to transfer, sell, tender or otherwise dispose of shares of common stock or such other securities in connection with such a change of control;

provided that in the case of any transfer, disposition or distribution pursuant to the second, third, fourth or fifth bullet (i) each transferee, donee or distributee shall agree to be subject to the restrictions described in the immediately preceding paragraph and (ii) no filing under Section 16(a) of the Exchange Act, reporting a reduction in beneficial ownership of shares of common stock, shall be required or shall be voluntarily made during the restricted period (other than, in the case of a transfer or other disposition pursuant to the third bullet above, any Form 4 or Form 5 required to be filed under the Exchange Act if the signatory is subject to Section 16 reporting with respect to us under the Exchange Act and indicating by footnote disclosure or otherwise the nature of the transfer or disposition).

The restrictions on transfers or other dispositions by us described in the paragraph above do not apply to:

- the shares to be sold in this offering;
- the issuance by us of shares of common stock upon the exercise of an option or a warrant or the conversion of a security outstanding on the date of this prospectus pursuant to stock plans disclosed in this prospectus;

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- the grant by us of any options to purchase shares of common stock or other awards granted under a stock incentive plan or stock purchase plan described in this prospectus, and the issuance by us of shares of common stock upon the exercise thereof, provided that we will cause each recipient of such grant to execute and deliver to the underwriters a lock-up agreement if such recipient has not already delivered one;
- the filing by the us of any registration statement on Form S-8 or a successor form thereto relating to the shares of common stock granted pursuant to or reserved for issuance under a stock incentive plan or stock purchase plan described in this prospectus; or
- shares of common stock or other securities issued in connection with a joint venture, equipment leasing arrangement, licensing or collaboration transaction or other strategic transaction with an unaffiliated third party, provided that (x) the aggregate number of shares issued pursuant to this exception will not exceed 5% of the total number of outstanding shares of common stock immediately following the issuance and sale of the shares to be sold in this offering and (y) the recipient of any such shares of common stock and securities issued pursuant to this exception during the restricted period will enter into a lock-up agreement.

Nasdaq Global Market Listing

Our common stock is listed on the Nasdaq Global Market under the symbol “FULC.”

Price Stabilization, Short Positions and Penalty Bids

Until the distribution of the shares is completed, SEC rules may limit underwriters and selling group members from bidding for and purchasing our common stock. However, the representatives may engage in transactions that stabilize the price of the common stock, such as bids or purchases to peg, fix or maintain that price.

In connection with this offering, the underwriters may purchase and sell our common stock in the open market. These transactions may include short sales, purchases on the open market to cover positions created by short sales and stabilizing transactions. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in this offering. “Covered” short sales are sales made in an amount not greater than the underwriters’ option to purchase additional shares described above. The underwriters may close out any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares granted to them under the underwriting agreement described above. “Naked” short sales are sales in excess of such option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of our common stock in the open market after pricing that could adversely affect investors who purchase in this offering. Stabilizing transactions consist of various bids for or purchases of shares of common stock made by the underwriters in the open market prior to the closing of this offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Similar to other purchase transactions, the underwriters’ purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. The underwriters may conduct these transactions on the Nasdaq Global Market, in the over-the-counter market or otherwise.

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Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. In addition, neither we nor any of the underwriters make any representation that the representatives will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Electronic Distribution

In connection with this offering, certain of the underwriters or securities dealers may distribute prospectuses by electronic means, such as e-mail.

Other Relationships

The underwriters and certain of their affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. Some of the underwriters and certain of their affiliates may in the future engage in investment banking and other commercial dealings in the ordinary course of business with us and our affiliates, for which they may in the future receive customary fees, commissions and expenses.

In addition, in the ordinary course of their business activities, the underwriters and their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Selling Restrictions

European Economic Area and the United Kingdom

In relation to each Member State of the European Economic Area and the United Kingdom, each referred to here as a Relevant State, no shares have been offered or will be offered pursuant to the offering to the public in that Relevant State prior to the publication of a prospectus in relation to the shares which has been approved by the competent authority in that Relevant State or, where appropriate, approved in another Relevant State and notified to the competent authority in that Relevant State, all in accordance with the Prospectus Regulation, except that offers of shares may be made to the public in that Relevant State at any time under the following exemptions under the Prospectus Regulation:

- A. to any legal entity which is a qualified investor as defined under the Prospectus Regulation;
- B. to fewer than 150 natural or legal persons (other than qualified investors as defined under the Prospectus Regulation), subject to obtaining the prior consent of the underwriters for any such offer; or
- C. in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of shares shall require us or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation.

Each person in a Relevant State who initially acquires any shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with us and the underwriters that it is a qualified investor within the meaning of the Prospectus Regulation and each person who initially acquires any shares or to whom any offer is

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made will be deemed to have represented, acknowledged and agreed to and with each of the underwriters and us that it is a “qualified investor” within the meaning of Article 2(e) of the Prospectus Regulation.

In the case of any shares being offered to a financial intermediary as that term is used in Article 5(1) of the Prospectus Regulation, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer to the public other than their offer or resale in a Relevant State to qualified investors, in circumstances in which the prior consent of the representatives has been obtained to each such proposed offer or resale.

We, the underwriters and each of our and the underwriters’ respective affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

For the purposes of this provision, the expression an “offer to the public” in relation to any shares in any Relevant State means the communication in any form and by any means of sufficient information on the terms of the offer and any shares to be offered so as to enable an investor to decide to purchase or subscribe for any shares, and the expression “Prospectus Regulation” means Regulation (EU) 2017/1129, as amended.

References to the Prospectus Regulation include, in relation to the United Kingdom, the Prospectus Regulation as it forms part of United Kingdom domestic law by virtue of the European Union (Withdrawal) Act 2018, as amended.

The above selling restriction is in addition to any other selling restrictions set out below.

Notice to Prospective Investors in the United Kingdom

In addition, in the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are “qualified investors” (as defined in the Prospectus Regulation) (i) who have professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended, or the Order, and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order, all such persons together being referred to as relevant persons, or otherwise in circumstances which have not resulted and will not result in an offer to the public of the shares in the United Kingdom within the meaning of the Financial Services and Markets Act 2000, as amended.

Any person in the United Kingdom that is not a relevant person should not act or rely on the information included in this document or use it as basis for taking any action. In the United Kingdom, any investment or investment activity that this document relates to may be made or taken exclusively by relevant persons.

Notice to Prospective Investors in Canada

The shares may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the shares must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus supplement (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the

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time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

LEGAL MATTERS

The validity of the shares of common stock offered hereby is being passed upon for us by Wilmer Cutler Pickering Hale and Dorr LLP, Boston, Massachusetts. Ropes & Gray LLP, Boston, Massachusetts is acting as counsel for the underwriters in connection with this offering.

EXPERTS

The consolidated financial statements of Fulcrum Therapeutics, Inc. appearing in Fulcrum Therapeutics, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2019, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at <http://www.sec.gov>. Copies of certain information filed by us with the SEC are also available on our website at <http://www.fulcrumtx.com>. Our website is not a part of this prospectus supplement and is not incorporated by reference in this prospectus supplement.

This prospectus supplement is part of a registration statement that we filed with the SEC. The registration statement contains more information than this prospectus supplement and the accompanying prospectus regarding us and the securities, including certain exhibits and schedules. You can obtain a copy of the registration statement from the SEC's internet site.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference into this prospectus supplement and the accompanying prospectus much of the information we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference into this prospectus supplement and the accompanying prospectus is considered to be part of this prospectus supplement and the accompanying prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus supplement and the accompanying prospectus is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus supplement and the accompanying prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus supplement, the accompanying prospectus or in any document previously incorporated by reference have been modified or superseded. This prospectus supplement and the accompanying prospectus incorporate by reference the documents listed below (File No. 001-38978) and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended (in each case, other than those documents or the portions of those documents not deemed to be filed), until the offering of the securities under the registration statement is terminated or completed:

- Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2019, including the information specifically incorporated by reference into the Annual Report on Form 10-K from our [definitive proxy statement](#) for the 2020 Annual Meeting of Stockholders;
- Quarterly Reports on Form 10-Q for the fiscal quarters ended [March 31, 2020](#), [June 30, 2020](#) and [September 30, 2020](#);

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- Current Reports on Form 8-K filed on [January 6, 2020](#), [April 2, 2020](#), [June 10, 2020](#) (other than Item 7.01), [June 11, 2020](#), [June 26, 2020](#) and [July 23, 2020](#); and
- The description of our common stock contained in our Registration Statement on [Form 8-A](#) filed on July 12, 2019, including any amendments or reports filed for the purpose of updating such description.

You may request a copy of these filings, at no cost, by writing or calling us at the following address or telephone number:

Fulcrum Therapeutics, Inc.
26 Landsdowne Street
Cambridge, Massachusetts 02139
Attn: Investor Relations
(617) 651-8851

S-26

PROSPECTUS

\$250,000,000



**Debt Securities
Common Stock
Preferred Stock
Depository Shares
Units
Warrants**

We may offer and sell up to \$250,000,000 in the aggregate of securities from time to time in one or more offerings. This prospectus describes the general terms of these securities and the general manner in which these securities will be offered. We will provide the specific terms of these securities in supplements to this prospectus. The prospectus supplements will also describe the specific manner in which these securities will be offered and may also supplement, update or amend information contained or incorporated by reference in this document. You should read this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as the documents incorporated by reference herein and therein, carefully before you invest.

We may offer these securities in amounts, at prices and on terms determined at the time of offering. The securities may be sold directly to you, through agents, or through underwriters and dealers. If agents, underwriters or dealers are used to sell the securities, we will name them and describe their compensation in a prospectus supplement.

Our common stock is listed on The Nasdaq Global Market under the symbol "FULC".

Investing in these securities involves significant risks. See "[Risk Factors](#)" included in any accompanying prospectus supplement and in the documents incorporated by reference in this prospectus for a discussion of the factors you should carefully consider before deciding to purchase these securities.

We may amend or supplement this prospectus from time to time by filing amendments or supplements as required. We urge you to read the entire prospectus, any amendments or supplements, any free writing prospectuses, and any documents incorporated by reference carefully before you make your investment decision.

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

The date of this prospectus is August 17, 2020

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, which we refer to as the “SEC,” utilizing a “shelf” registration process. Under this shelf registration process, we may from time to time sell any combination of the securities described in this prospectus in one or more offerings for an aggregate initial offering price of up to \$250,000,000.

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide one or more prospectus supplements that will contain specific information about the terms of the offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. The prospectus supplement may also add, update or change information contained in this prospectus or in any documents that we have incorporated by reference into this prospectus and, accordingly, to the extent inconsistent, information in this prospectus is superseded by the information in the prospectus supplement or any related free writing prospectus. You should read both this prospectus and the accompanying prospectus supplement together with the additional information described under the heading “Where You Can Find More Information” on page 2 of this prospectus.

We have not authorized anyone to provide you with any information other than that contained or incorporated by reference in this prospectus or any accompanying prospectus supplement or free writing prospectus to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information others may give you. This prospectus and any accompanying prospectus supplement do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in this prospectus or such accompanying prospectus supplement or an offer to sell or the solicitation of an offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. You should assume that the information appearing in this prospectus, any prospectus supplement, the documents incorporated by reference and any related free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

No offer of these securities will be made in any jurisdiction where the offer is not permitted.

Unless the context otherwise indicates, references in this prospectus to “we,” “our” and “us” refer, collectively, to Fulcrum Therapeutics, Inc., a Delaware corporation, and its consolidated subsidiary.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at <http://www.sec.gov>. Copies of certain information filed by us with the SEC are also available on our website at <http://www.fulcrumtx.com>. Our website is not a part of this prospectus and information contained on, or that can be accessed through our website, is not incorporated by reference in this prospectus.

This prospectus is part of a registration statement we filed with the SEC. This prospectus omits some information contained in the registration statement in accordance with SEC rules and regulations. You should review the information and exhibits in the registration statement for further information about us and our consolidated subsidiary and the securities we are offering. Statements in this prospectus concerning any document we filed as an exhibit to the registration statement or that we otherwise filed with the SEC are not intended to be comprehensive and are qualified by reference to these filings. You should review the complete document to evaluate these statements. You can obtain a copy of the registration statement from the SEC's website.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to incorporate by reference much of the information we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus is considered to be part of this prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus or in any document previously incorporated by reference have been modified or superseded. This prospectus incorporates by reference the documents listed below (File No. 001-38978) and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act (in each case, other than those documents or the portions of those documents not deemed to be filed) between the date of the initial registration statement and the effectiveness of the registration statement and following the effectiveness of the registration statement until the offering of the securities under the registration statement is terminated or completed:

- Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2019, including the information specifically incorporated by reference into the Annual Report on Form 10-K from our [definitive proxy statement](#) for the 2020 Annual Meeting of Stockholders;
- Quarterly Reports on Form 10-Q for the fiscal quarters ended [March 31, 2020](#) and [June 30, 2020](#);
- Current Reports on Form 8-K filed on [January 6, 2020](#), [April 2, 2020](#), [June 10, 2020](#), [June 11, 2020](#), [June 26, 2020](#) and [July 23, 2020](#); and
- The description of our common stock contained in our Registration Statement on [Form 8-A](#) filed on July 12, 2019, including any amendments or reports filed for the purpose of updating such description.

You may request a copy of these filings, at no cost, by writing or calling us at the following address or telephone number:

Fulcrum Therapeutics, Inc.
26 Landsdowne Street
Cambridge, Massachusetts 02139
Attn: Investor Relations
(617) 651-8851

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This prospectus and the documents incorporated by reference in this prospectus include “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Exchange Act. All statements, other than statements of historical fact, contained or incorporated by reference in this prospectus, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “might,” “plan,” “predict,” “project,” “target,” “potential,” “would,” “could,” “should,” “continue” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

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, or incorporated by reference, in this prospectus, particularly in the “Risk Factors” section, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. You should also carefully review the risk factors and cautionary statements described in the other documents we file from time to time with the SEC, specifically our most recent Annual Report on Form 10-K, our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

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

This prospectus includes or incorporates by reference certain 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. 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.

ABOUT FULCRUM THERAPEUTICS, INC.

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.

Corporate Information

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

We own or have rights, or have applied for, to trademarks, service marks and trade names that we use in connection with the operation of our business, including our corporate name, logos and website names. Other trademarks, service marks and trade names appearing in this prospectus are the property of their respective owners. Solely for convenience, some of the trademarks, service marks and trade names referred to in this prospectus are listed without the ® and ™ symbols, but we will assert, to the fullest extent under applicable law, our rights to our trademarks, service marks and trade names.

RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully consider the risks and uncertainties described under “Risk Factors” in our most recent Annual Report on Form 10-K, our most recent Quarterly Report on Form 10-Q and in any accompanying prospectus supplement, together with all of the other information included or incorporated by reference in this prospectus and in any accompanying prospectus supplement, including our consolidated financial statements and related notes, before deciding whether to purchase our securities.

Our business, financial condition and results of operations could be materially and adversely affected by any or all of these risks or by additional risks and uncertainties not presently known to us or that we currently deem immaterial that may adversely affect us in the future.

USE OF PROCEEDS

We intend to use the net proceeds from the sale of any securities offered under this prospectus for general corporate purposes unless otherwise indicated in the applicable prospectus supplement. General corporate purposes may include working capital and capital expenditures, research and development expenses, including clinical trial costs, general and administrative expenses, potential acquisition of, or investment in, companies, technologies, products or assets that complement our business, and repayment and refinancing of debt. We have not determined the amount of net proceeds to be used specifically for such purposes. As a result, management will retain broad discretion over the allocation of net proceeds.

DESCRIPTION OF DEBT SECURITIES

We may offer debt securities which may be senior or subordinated. We refer to the senior debt securities and the subordinated debt securities collectively as debt securities. The following description summarizes the general terms and provisions of the debt securities. We will describe the specific terms of the debt securities and the extent, if any, to which the general provisions summarized below apply to any series of debt securities in the prospectus supplement relating to the series and any applicable free writing prospectus that we authorize to be delivered. When we refer to “the Company,” “we,” “our,” and “us” in this section, we mean Fulcrum Therapeutics, Inc. excluding, unless the context otherwise requires or as otherwise expressly stated, our subsidiary.

We may issue senior debt securities from time to time, in one or more series under a senior indenture to be entered into between us and a senior trustee to be named in a prospectus supplement, which we refer to as the senior trustee. We may issue subordinated debt securities from time to time, in one or more series under a subordinated indenture to be entered into between us and a subordinated trustee to be named in a prospectus supplement, which we refer to as the subordinated trustee. The forms of senior indenture and subordinated indenture are filed as exhibits to the registration statement of which this prospectus forms a part. The senior indenture and the subordinated indenture are referred to individually as an indenture and together as the indentures and the senior trustee and the subordinated trustee are referred to individually as a trustee and together as the trustees. This section summarizes some of the provisions of the indentures and is qualified in its entirety by the specific text of the indentures, including definitions of terms used in the indentures. Wherever we refer to particular sections of, or defined terms in, the indentures, those sections or defined terms are incorporated by reference in this prospectus or the applicable prospectus supplement. You should review the indentures that are filed as exhibits to the registration statement of which this prospectus forms a part for additional information.

Neither indenture will limit the amount of debt securities that we may issue. The applicable indenture will provide that debt securities may be issued up to an aggregate principal amount authorized from time to time by us and may be payable in any currency or currency unit designated by us or in amounts determined by reference to an index.

General

The senior debt securities will constitute our unsecured and unsubordinated general obligations and will rank equally in right of payment with our other unsecured and unsubordinated obligations. The subordinated debt securities will constitute our unsecured and subordinated general obligations and will be junior in right of payment to our senior indebtedness (including senior debt securities), as described under the heading “—Certain Terms of the Subordinated Debt Securities—Subordination.” The debt securities will be structurally subordinated to all existing and future indebtedness and other liabilities of our subsidiary unless such subsidiary expressly guarantee such debt securities.

The debt securities will be our unsecured obligations. Any secured debt or other secured obligations will be effectively senior to the debt securities to the extent of the value of the assets securing such debt or other obligations. Unless otherwise indicated in the applicable prospectus supplement, the debt securities will not be guaranteed by our subsidiary.

The applicable prospectus supplement and/or free writing prospectus will include any additional or different terms of the debt securities of any series being offered, including the following terms:

- the title and type of the debt securities;
- whether the debt securities will be senior or subordinated debt securities, and, with respect to any subordinated debt securities the terms on which they are subordinated;
- the initial aggregate principal amount of the debt securities;

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- the price or prices at which we will sell the debt securities;
- the maturity date or dates of the debt securities and the right, if any, to extend such date or dates;
- the rate or rates, if any, at which the debt securities will bear interest, or the method of determining such rate or rates;
- the date or dates from which such interest will accrue, the interest payment dates on which such interest will be payable or the method of determination of such dates;
- the right, if any, to extend the interest payment periods and the duration of that extension;
- the manner of paying principal and interest and the place or places where principal and interest will be payable;
- provisions for a sinking fund, purchase fund or other analogous fund, if any;
- any redemption dates, prices, obligations and restrictions on the debt securities;
- the currency, currencies or currency units in which the debt securities will be denominated and the currency, currencies or currency units in which principal and interest, if any, on the debt securities may be payable;
- any conversion or exchange features of the debt securities;
- whether the debt securities will be subject to the defeasance provisions in the indenture;
- whether the debt securities will be issued in definitive or global form or in definitive form only upon satisfaction of certain conditions;
- whether the debt securities will be guaranteed as to payment or performance;
- any special tax implications of the debt securities;
- any events of defaults or covenants in addition to or in lieu of those set forth in the indenture; and
- any other material terms of the debt securities.

When we refer to “principal” in this section with reference to the debt securities, we are also referring to “premium, if any.”

We may from time to time, without notice to or the consent of the holders of any series of debt securities, create and issue further debt securities of any such series ranking equally with the debt securities of such series in all respects (or in all respects other than (1) the payment of interest accruing prior to the issue date of such further debt securities or (2) the first payment of interest following the issue date of such further debt securities). Such further debt securities may be consolidated and form a single series with the debt securities of such series and have the same terms as to status, redemption or otherwise as the debt securities of such series.

You may present debt securities for exchange and you may present debt securities for transfer in the manner, at the places and subject to the restrictions set forth in the debt securities and the applicable prospectus supplement. We will provide you those services without charge, although you may have to pay any tax or other governmental charge payable in connection with any exchange or transfer, as set forth in the indenture.

Debt securities may bear interest at a fixed rate or a floating rate. Debt securities bearing no interest or interest at a rate that at the time of issuance is below the prevailing market rate (original issue discount securities) may be sold at a discount below their stated principal amount. U.S. federal income tax considerations applicable to any such discounted debt securities or to certain debt securities issued at par which are treated as having been issued at a discount for U.S. federal income tax purposes will be described in the applicable prospectus supplement.

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We may issue debt securities with the principal amount payable on any principal payment date, or the amount of interest payable on any interest payment date, to be determined by reference to one or more currency exchange rates, securities or baskets of securities, commodity prices or indices. You may receive a payment of principal on any principal payment date, or a payment of interest on any interest payment date, that is greater than or less than the amount of principal or interest otherwise payable on such dates, depending on the value on such dates of the applicable currency, security or basket of securities, commodity or index. Information as to the methods for determining the amount of principal or interest payable on any date, the currencies, securities or baskets of securities, commodities or indices to which the amount payable on such date is linked and certain related tax considerations will be set forth in the applicable prospectus supplement.

Certain Terms of the Senior Debt Securities

Covenants. Unless we indicate otherwise in a prospectus supplement with respect to a particular series of senior debt securities, the senior debt securities will not contain any financial or restrictive covenants, including covenants restricting either us or our subsidiary from incurring, issuing, assuming or guaranteeing any indebtedness secured by a lien on any of our or our subsidiary's property or capital stock, or restricting either us or our subsidiary from entering into sale and leaseback transactions.

Consolidation, Merger and Sale of Assets. Unless we indicate otherwise in a prospectus supplement with respect to a particular series of senior debt securities, we may not consolidate with or merge into any other person, in a transaction in which we are not the surviving corporation, or convey, transfer or lease our properties and assets substantially as an entirety to any person, in either case, unless:

- the successor entity, if any, is a U.S. corporation, limited liability company, partnership or trust;
- the successor entity assumes our obligations on the senior debt securities and under the senior indenture;
- immediately after giving effect to the transaction, no default or event of default shall have occurred and be continuing; and
- we have delivered to the senior trustee an officer's certificate and an opinion of counsel, each stating that the consolidation, merger, conveyance, transfer or lease and, if a supplemental indenture is required in connection with such transaction, such supplemental indenture, comply with the senior indenture and all conditions precedent provided for in the senior indenture relating to such transaction have been complied with.

The restrictions described in the bullets above do not apply (1) to our consolidation with or merging into one of our affiliates, if our board of directors determines in good faith that the purpose of the consolidation or merger is principally to change our state of incorporation or our form of organization to another form or (2) if we merge with or into a single direct or indirect wholly-owned subsidiary of ours.

The surviving business entity will succeed to, and be substituted for, us under the senior indenture and the senior debt securities and, except in the case of a lease, we shall be released from all obligations under the senior indenture and the senior debt securities.

No Protection in the Event of a Change in Control. Unless we indicate otherwise in a prospectus supplement with respect to a particular series of senior debt securities, the senior debt securities will not contain any provisions that may afford holders of the senior debt securities protection in the event we have a change in control or in the event of a highly leveraged transaction (whether or not such transaction results in a change in control).

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Events of Default. Unless we indicate otherwise in a prospectus supplement with respect to a particular series of senior debt securities, the following are events of default under the senior indenture with respect to senior debt securities of each series:

- failure to pay interest on any senior debt securities of such series when due and payable, if that default continues for a period of 30 days (or such other period as may be specified for such series);
- failure to pay principal on the senior debt securities of such series when due and payable whether at maturity, upon redemption, by declaration or otherwise (and, if specified for such series, the continuance of such failure for a specified period);
- default in the performance of or breach of any of our covenants or agreements in the senior indenture applicable to senior debt securities of such series, other than a covenant breach which is specifically dealt with elsewhere in the senior indenture, and that default or breach continues for a period of 90 days after we receive written notice from the trustee or from the holders of 25% or more in aggregate principal amount of the senior debt securities of such series;
- certain events of bankruptcy or insolvency, whether or not voluntary; and
- any other event of default provided for in such series of senior debt securities as may be specified in the applicable prospectus supplement.

The default by us under any other debt, including any other series of debt securities, is not a default under the senior indenture.

If an event of default other than an event of default specified in the fourth bullet point above occurs with respect to a series of senior debt securities and is continuing under the senior indenture, then, and in each such case, either the trustee or the holders of not less than 25% in aggregate principal amount of such series then outstanding under the senior indenture (each such series voting as a separate class) by written notice to us and to the trustee, if such notice is given by the holders, may, and the trustee at the request of such holders shall, declare the principal amount of and accrued interest on such series of senior debt securities to be immediately due and payable, and upon this declaration, the same shall become immediately due and payable.

If an event of default specified in the fourth bullet point above occurs and is continuing, the entire principal amount of and accrued interest on each series of senior debt securities then outstanding shall automatically become immediately due and payable.

Unless otherwise specified in the prospectus supplement relating to a series of senior debt securities originally issued at a discount, the amount due upon acceleration shall include only the original issue price of the senior debt securities, the amount of original issue discount accrued to the date of acceleration and accrued interest, if any.

Upon certain conditions, declarations of acceleration may be rescinded and annulled and past defaults may be waived by the holders of a majority in aggregate principal amount of all the senior debt securities of such series affected by the default, each series voting as a separate class. Furthermore, subject to various provisions in the senior indenture, the holders of a majority in aggregate principal amount of a series of senior debt securities, by notice to the trustee, may waive a continuing default or event of default with respect to such senior debt securities and its consequences, except a default in the payment of principal of or interest on such senior debt securities (other than any such default in payment resulting solely from an acceleration of the senior debt securities) or in respect of a covenant or provision of the senior indenture which cannot be modified or amended without the consent of the holders of each such senior debt security. Upon any such waiver, such default shall cease to exist, and any event of default with respect to such senior debt securities shall be deemed to have been cured, for every purpose of the senior indenture; but no such waiver shall extend to any subsequent or other default or event of default or impair any right consequent thereto.

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The holders of a majority in aggregate principal amount of a series of senior debt securities may direct the time, method and place of conducting any proceeding for any remedy available to the trustee or exercising any trust or power conferred on the trustee with respect to such senior debt securities. However, the trustee may refuse to follow any direction that conflicts with law or the senior indenture, that may involve the trustee in personal liability or that the trustee determines in good faith may be unduly prejudicial to the rights of holders of such series of senior debt securities not joining in the giving of such direction and may take any other action it deems proper that is not inconsistent with any such direction received from holders of such series of senior debt securities. A holder may not pursue any remedy with respect to the senior indenture or any series of senior debt securities unless:

- the holder gives the trustee written notice of a continuing event of default;
- the holders of at least 25% in aggregate principal amount of such series of senior debt securities make a written request to the trustee to pursue the remedy in respect of such event of default;
- the requesting holder or holders offer the trustee indemnity satisfactory to the trustee against any costs, liability or expense;
- the trustee does not comply with the request within 60 days after receipt of the request and the offer of indemnity; and
- during such 60-day period, the holders of a majority in aggregate principal amount of such series of senior debt securities do not give the trustee a direction that is inconsistent with the request.

These limitations, however, do not apply to the right of any holder of a senior debt security of any affected series to receive payment of the principal of and interest on such senior debt security in accordance with the terms of such debt security, or to bring suit for the enforcement of any such payment in accordance with the terms of such debt security, on or after the due date for the senior debt securities, which right shall not be impaired or affected without the consent of the holder.

The senior indenture requires certain of our officers to certify, on or before a fixed date in each year in which any senior debt security is outstanding, as to their knowledge of our compliance with all covenants, agreements and conditions under the senior indenture.

Satisfaction and Discharge. We can satisfy and discharge our obligations to holders of any series of debt securities if:

- we have paid or caused to be paid the principal of and interest on all senior debt securities of such series (with certain limited exceptions) when due and payable; or
- we deliver to the senior trustee for cancellation all senior debt securities of such series theretofore authenticated under the senior indenture (with certain limited exceptions); or
- all senior debt securities of such series have become due and payable or will become due and payable within one year (or are to be called for redemption within one year under arrangements satisfactory to the senior trustee) and we deposit in trust an amount of cash or a combination of cash and U.S. government or U.S. government agency obligations (or in the case of senior debt securities denominated in a foreign currency, foreign government securities or foreign government agency securities) sufficient to make interest, principal and any other payments on the debt securities of that series on their various due dates;

and if, in any such case, we also pay or cause to be paid all other sums payable under the senior indenture, as and when the same shall be due and payable and we deliver to the senior trustee an officer's certificate and an opinion of counsel, each stating that these conditions have been satisfied.

Under current U.S. federal income tax law, the deposit and our legal release from the debt securities would be treated as though we took back your debt securities and gave you your share of the cash and debt securities or

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bonds deposited in trust. In that event, you could recognize gain or loss on the debt securities you give back to us. Purchasers of the debt securities should consult their own advisers with respect to the tax consequences to them of such deposit and discharge, including the applicability and effect of tax laws other than the U.S. federal income tax law.

Defeasance. Unless the applicable prospectus supplement provides otherwise, the following discussion of legal defeasance and covenant defeasance will apply to any series of debt securities issued under the indentures.

Legal Defeasance. We can legally release ourselves from any payment or other obligations on the debt securities of any series (called “legal defeasance”) if certain conditions are met, including the following:

- We deposit in trust for your benefit and the benefit of all other direct holders of the debt securities of the same series cash or a combination of cash and U.S. government or U.S. government agency obligations (or, in the case of senior debt securities denominated in a foreign currency, foreign government or foreign government agency obligations) that will generate enough cash to make interest, principal and any other payments on the debt securities of that series on their various due dates.
- There is a change in current U.S. federal income tax law or an IRS ruling that lets us make the above deposit without causing you to be taxed on the debt securities any differently than if we did not make the deposit and instead repaid the debt securities ourselves when due. Under current U.S. federal income tax law, the deposit and our legal release from the debt securities would be treated as though we took back your debt securities and gave you your share of the cash and debt securities or bonds deposited in trust. In that event, you could recognize gain or loss on the debt securities you give back to us.
- We deliver to the trustee a legal opinion of our counsel confirming the tax law change or ruling described above.

If we accomplish legal defeasance, as described above, you would have to rely solely on the trust deposit for repayment of the debt securities. You could not look to us for repayment in the event of any shortfall.

Covenant Defeasance. Without any change in current U.S. federal tax law, we can make the same type of deposit described above and be released from some of the covenants in the debt securities (called “covenant defeasance”). In that event, you would lose the protection of those covenants but would gain the protection of having money and securities set aside in trust to repay the debt securities. In order to achieve covenant defeasance, we must do the following (among other things):

- We must deposit in trust for your benefit and the benefit of all other direct holders of the debt securities of the same series cash or a combination of cash and U.S. government or U.S. government agency obligations (or, in the case of senior debt securities denominated in a foreign currency, foreign government or foreign government agency obligations) that will generate enough cash to make interest, principal and any other payments on the debt securities of that series on their various due dates.
- We must deliver to the trustee a legal opinion of our counsel confirming that under current U.S. federal income tax law we may make the above deposit without causing you to be taxed on the debt securities any differently than if we did not make the deposit and instead repaid the debt securities ourselves when due.

If we accomplish covenant defeasance, you could still look to us for repayment of the debt securities if there were a shortfall in the trust deposit. In fact, if one of the events of default occurred (such as our bankruptcy) and the debt securities become immediately due and payable, there may be such a shortfall. Depending on the events causing the default, you may not be able to obtain payment of the shortfall.

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Modification and Waiver. We and the trustee may amend or supplement the senior indenture or the senior debt securities of any series without the consent of any holder:

- to convey, transfer, assign, mortgage or pledge any assets as security for the senior debt securities of one or more series;
- to evidence the succession of a corporation, limited liability company, partnership or trust to us, and the assumption by such successor of our covenants, agreements and obligations under the senior indenture or to otherwise comply with the covenant relating to mergers, consolidations and sales of assets;
- to comply with the requirements of the SEC in order to effect or maintain the qualification of the senior indenture under the Trust Indenture Act of 1939, as amended (the “Trust Indenture Act”);
- to add to our covenants such new covenants, restrictions, conditions or provisions for the protection of the holders, and to make the occurrence, or the occurrence and continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default;
- to cure any ambiguity, defect or inconsistency in the senior indenture or in any supplemental indenture or to conform the senior indenture or the senior debt securities to the description of senior debt securities of such series set forth in this prospectus or any applicable prospectus supplement;
- to provide for or add guarantors with respect to the senior debt securities of any series;
- to establish the form or forms or terms of the senior debt securities as permitted by the senior indenture;
- to evidence and provide for the acceptance of appointment under the senior indenture by a successor trustee, or to make such changes as shall be necessary to provide for or facilitate the administration of the trusts in the senior indenture by more than one trustee;
- to add to, change or eliminate any of the provisions of the senior indenture in respect of one or more series of senior debt securities, provided that any such addition, change or elimination shall (a) neither (1) apply to any senior debt security of any series created prior to the execution of such supplemental indenture and entitled to the benefit of such provision nor (2) modify the rights of the holder of any such senior debt security with respect to such provision or (b) become effective only when there is no senior debt security described in clause (a)(1) outstanding;
- to make any change to the senior debt securities of any series so long as no senior debt securities of such series are outstanding; or
- to make any change that does not adversely affect the rights of any holder in any material respect.

Other amendments and modifications of the senior indenture or the senior debt securities issued may be made, and our compliance with any provision of the senior indenture with respect to any series of senior debt securities may be waived, with the consent of the holders of a majority of the aggregate principal amount of the outstanding senior debt securities of each series affected by the amendment or modification (voting as separate series); provided, however, that each affected holder must consent to any modification, amendment or waiver that:

- extends the final maturity of any senior debt securities of such series;
- reduces the principal amount of any senior debt securities of such series;
- reduces the rate, or extends the time for payment of, interest on any senior debt securities of such series;
- reduces the amount payable upon the redemption of any senior debt securities of such series;
- changes the currency of payment of principal of or interest on any senior debt securities of such series;

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- reduces the principal amount of original issue discount securities payable upon acceleration of maturity or the amount provable in bankruptcy;
- waives a continuing default in the payment of principal of or interest on the senior debt securities (other than any such default in payment resulting solely from an acceleration of the senior debt securities);
- changes the provisions relating to the waiver of past defaults or impairs the right of holders to receive payment or to institute suit for the enforcement of any payment or conversion of any senior debt securities of such series on or after the due date therefor;
- modifies any of the provisions of these restrictions on amendments and modifications, except to increase any required percentage or to provide that certain other provisions cannot be modified or waived without the consent of the holder of each senior debt security of such series affected by the modification;
- adversely affects the right to convert or exchange senior debt securities into common stock or other property in accordance with the terms of the senior debt securities; or
- reduces the above-stated percentage of outstanding senior debt securities of such series whose holders must consent to a supplemental indenture or modifies or amends or waives certain provisions of or defaults under the senior indenture.

It shall not be necessary for the holders to approve the particular form of any proposed amendment, supplement or waiver, but it shall be sufficient if the holders' consent approves the substance thereof. After an amendment, supplement or waiver of the senior indenture in accordance with the provisions described in this section becomes effective, the trustee must give to the holders affected thereby certain notice briefly describing the amendment, supplement or waiver. Any failure by the trustee to give such notice, or any defect therein, shall not, however, in any way impair or affect the validity of any such amendment, supplemental indenture or waiver.

No Personal Liability of Incorporators, Stockholders, Officers or Directors. The senior indenture provides that no recourse shall be had under any obligation, covenant or agreement of ours in the senior indenture or any supplemental indenture, or in any of the senior debt securities or because of the creation of any indebtedness represented thereby, against any of our incorporators, stockholders, officers or directors, past, present or future, or of any predecessor or successor entity thereof under any law, statute or constitutional provision or by the enforcement of any assessment or by any legal or equitable proceeding or otherwise. Each holder, by accepting the senior debt securities, waives and releases all such liability.

Concerning the Trustee. The senior indenture provides that, except during the continuance of an event of default, the trustee will not be liable except for the performance of such duties as are specifically set forth in the senior indenture. If an event of default has occurred and is continuing, the trustee will exercise such rights and powers vested in it under the senior indenture and will use the same degree of care and skill in its exercise as a prudent person would exercise under the circumstances in the conduct of such person's own affairs.

The senior indenture and the provisions of the Trust Indenture Act incorporated by reference therein contain limitations on the rights of the trustee thereunder, should it become a creditor of ours or our subsidiary, to obtain payment of claims in certain cases or to realize on certain property received by it in respect of any such claims, as security or otherwise. The trustee is permitted to engage in other transactions, provided that if it acquires any conflicting interest (as defined in the Trust Indenture Act), it must eliminate such conflict or resign.

We may have normal banking relationships with the senior trustee in the ordinary course of business.

Unclaimed Funds. All funds deposited with the trustee or any paying agent for the payment of principal, premium, interest or additional amounts in respect of the senior debt securities that remain unclaimed for

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two years after the date upon which such amounts became due and payable will be repaid to us. Thereafter, any right of any holder of senior debt securities to such funds shall be enforceable only against us, and the trustee and paying agents will have no liability therefor.

Governing Law. The senior indenture and the senior debt securities will be governed by, and construed in accordance with, the internal laws of the State of New York.

Certain Terms of the Subordinated Debt Securities

Other than the terms of the subordinated indenture and subordinated debt securities relating to subordination or otherwise as described in the prospectus supplement relating to a particular series of subordinated debt securities, the terms of the subordinated indenture and subordinated debt securities are identical in all material respects to the terms of the senior indenture and senior debt securities.

Additional or different subordination terms may be specified in the prospectus supplement applicable to a particular series.

Subordination. The indebtedness evidenced by the subordinated debt securities is subordinate to the prior payment in full of all of our senior indebtedness, as defined in the subordinated indenture. During the continuance beyond any applicable grace period of any default in the payment of principal, premium, interest or any other payment due on any of our senior indebtedness, we may not make any payment of principal or interest on the subordinated debt securities (except for certain sinking fund payments). In addition, upon any payment or distribution of our assets upon any dissolution, winding-up, liquidation or reorganization, the payment of the principal of and interest on the subordinated debt securities will be subordinated to the extent provided in the subordinated indenture in right of payment to the prior payment in full of all our senior indebtedness. Because of this subordination, if we dissolve or otherwise liquidate, holders of our subordinated debt securities may receive less, ratably, than holders of our senior indebtedness. The subordination provisions do not prevent the occurrence of an event of default under the subordinated indenture.

The term “senior indebtedness” of a person means with respect to such person the principal of, premium, if any, interest on, and any other payment due pursuant to any of the following, whether outstanding on the date of the subordinated indenture or incurred by that person in the future:

- all of the indebtedness of that person for money borrowed;
- all of the indebtedness of that person evidenced by notes, debentures, bonds or other securities sold by that person for money;
- all of the lease obligations that are capitalized on the books of that person in accordance with generally accepted accounting principles;
- all indebtedness of others of the kinds described in the first two bullet points above and all lease obligations of others of the kind described in the third bullet point above that the person, in any manner, assumes or guarantees or that the person in effect guarantees through an agreement to purchase, whether that agreement is contingent or otherwise; and
- all renewals, extensions or refundings of indebtedness of the kinds described in the first, second or fourth bullet point above and all renewals or extensions of leases of the kinds described in the third or fourth bullet point above;

unless, in the case of any particular indebtedness, renewal, extension or refunding, the instrument creating or evidencing it or the assumption or guarantee relating to it expressly provides that such indebtedness, renewal, extension or refunding is not superior in right of payment to the subordinated debt securities. Our senior debt securities constitute senior indebtedness for purposes of the subordinated indenture.

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock and provisions of our certificate of incorporation and bylaws are summaries. You should also refer to the restated certificate of incorporation and the amended and restated bylaws, which are filed as exhibits to the registration statement of which this prospectus is part.

Our authorized capital stock consists of 200,000,000 shares of our common stock, par value \$0.001 per share, and 5,000,000 shares of our preferred stock, par value \$0.001 per share, all of which preferred stock is undesignated.

As of June 30, 2020, we had issued and outstanding 27,452,872 shares of our common stock held by 75 stockholders of record (not including beneficial owners whose shares are held in “nominee” or “street” name), including 229,076 shares of unvested restricted stock subject to repurchase by us.

Common Stock

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. Each election of directors by our stockholders will be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Any matters other than the election of directors to be voted upon by the stockholders at a meeting are decided by the vote of the holders of shares of stock having a majority in voting power of the votes cast by the holders of all of the shares of stock present or represented at the meeting and voting affirmatively or negatively on such matter, except when a different vote is required by law, our certificate of incorporation or our bylaws. Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend or other rights of any outstanding preferred stock.

In the event of our liquidation, dissolution or winding up, the holders of our common stock are entitled to receive proportionately all assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to any preferential or other rights of any outstanding preferred stock. Holders of our common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of holders of our common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of our preferred stock that we may designate and issue in the future.

Preferred Stock

We are authorized to issue “blank check” preferred stock, which may be issued in one or more series upon authorization of our board of directors. Our board of directors is authorized to fix the designations, powers, preferences and the relative, participating, optional or other special rights and any qualifications, limitations and restrictions of the shares of each series of preferred stock. The authorized shares of our preferred stock are available for issuance without further action by our stockholders, unless such action is required by applicable law or the rules of any stock exchange on which our securities may be listed. If the approval of our stockholders is not required for the issuance of shares of our preferred stock, our board may determine not to seek stockholder approval. The specific terms of any series of preferred stock offered pursuant to this prospectus will be described in the prospectus supplement relating to that series of preferred stock.

A series of our preferred stock could, depending on the terms of such series, impede the completion of a merger, tender offer or other takeover attempt. Our board of directors will make any determination to issue preferred shares based upon its judgment as to the best interests of our stockholders. Our directors, in so acting, could issue preferred stock having terms that could discourage an acquisition attempt through which an acquirer may be able to change the composition of our board of directors, including a tender offer or other transaction that some, or a majority, of our stockholders might believe to be in their best interests or in which stockholders might receive a premium for their stock over the then-current market price of the stock.

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The preferred stock has the terms described below unless otherwise provided in the prospectus supplement relating to a particular series of preferred stock. You should read the prospectus supplement relating to the particular series of preferred stock being offered for specific terms, including:

- the designation and stated value per share of the preferred stock and the number of shares offered;
- the amount of liquidation preference per share;
- the price at which the preferred stock will be issued;
- the dividend rate, or method of calculation of dividends, the dates on which dividends will be payable, whether dividends will be cumulative or noncumulative and, if cumulative, the dates from which dividends will commence to accumulate;
- any redemption or sinking fund provisions;
- if other than the currency of the United States, the currency or currencies including composite currencies in which the preferred stock is denominated and/or in which payments will or may be payable;
- any conversion provisions;
- whether we have elected to offer depositary shares as described under “Description of Depositary Shares;” and
- any other rights, preferences, privileges, limitations and restrictions on the preferred stock.

The preferred stock will, when issued, be fully paid and non-assessable. Unless otherwise specified in the prospectus supplement, each series of preferred stock will rank equally as to dividends and liquidation rights in all respects with each other series of preferred stock. The rights of holders of shares of each series of preferred stock will be subordinate to those of our general creditors.

As described under “Description of Depositary Shares,” we may, at our option, with respect to any series of preferred stock, elect to offer fractional interests in shares of preferred stock, and provide for the issuance of depositary receipts representing depositary shares, each of which will represent a fractional interest in a share of the series of preferred stock. The fractional interest will be specified in the prospectus supplement relating to a particular series of preferred stock.

Rank. Unless otherwise specified in the prospectus supplement, the preferred stock will, with respect to dividend rights and rights upon our liquidation, dissolution or winding up of our affairs, rank:

- senior to our common stock and to all equity securities ranking junior to such preferred stock with respect to dividend rights or rights upon our liquidation, dissolution or winding up of our affairs;
- on a parity with all equity securities issued by us, the terms of which specifically provide that such equity securities rank on a parity with the preferred stock with respect to dividend rights or rights upon our liquidation, dissolution or winding up of our affairs; and
- junior to all equity securities issued by us, the terms of which specifically provide that such equity securities rank senior to the preferred stock with respect to dividend rights or rights upon our liquidation, dissolution or winding up of our affairs.

The term “equity securities” does not include convertible debt securities.

Dividends. Holders of the preferred stock of each series will be entitled to receive, when, as and if declared by our board of directors, cash dividends at such rates and on such dates described in the prospectus supplement.

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Different series of preferred stock may be entitled to dividends at different rates or based on different methods of calculation. The dividend rate may be fixed or variable or both. Dividends will be payable to the holders of record as they appear on our stock books on record dates fixed by our board of directors, as specified in the applicable prospectus supplement.

Dividends on any series of preferred stock may be cumulative or noncumulative, as described in the applicable prospectus supplement. If our board of directors does not declare a dividend payable on a dividend payment date on any series of noncumulative preferred stock, then the holders of that noncumulative preferred stock will have no right to receive a dividend for that dividend payment date, and we will have no obligation to pay the dividend accrued for that period, whether or not dividends on that series are declared payable on any future dividend payment dates. Dividends on any series of cumulative preferred stock will accrue from the date we initially issue shares of such series or such other date specified in the applicable prospectus supplement.

No dividends may be declared or paid or funds set apart for the payment of any dividends on any parity securities unless full dividends have been paid or set apart for payment on the preferred stock. If full dividends are not paid, the preferred stock will share dividends pro rata with the parity securities.

No dividends may be declared or paid or funds set apart for the payment of dividends on any junior securities unless full dividends for all dividend periods terminating on or prior to the date of the declaration or payment will have been paid or declared and a sum sufficient for the payment set apart for payment on the preferred stock.

Liquidation Preference. Upon any voluntary or involuntary liquidation, dissolution or winding up of our affairs, then, before we make any distribution or payment to the holders of any common stock or any other class or series of our capital stock ranking junior to the preferred stock in the distribution of assets upon any liquidation, dissolution or winding up of our affairs, the holders of each series of preferred stock shall be entitled to receive out of assets legally available for distribution to stockholders, liquidating distributions in the amount of the liquidation preference per share set forth in the prospectus supplement, plus any accrued and unpaid dividends thereon. Such dividends will not include any accumulation in respect of unpaid noncumulative dividends for prior dividend periods. Unless otherwise specified in the prospectus supplement, after payment of the full amount of their liquidating distributions, the holders of preferred stock will have no right or claim to any of our remaining assets. Upon any such voluntary or involuntary liquidation, dissolution or winding up, if our available assets are insufficient to pay the amount of the liquidating distributions on all outstanding preferred stock and the corresponding amounts payable on all other classes or series of our capital stock ranking on parity with the preferred stock and all other such classes or series of shares of capital stock ranking on parity with the preferred stock in the distribution of assets, then the holders of the preferred stock and all other such classes or series of capital stock will share ratably in any such distribution of assets in proportion to the full liquidating distributions to which they would otherwise be entitled.

Upon any such liquidation, dissolution or winding up and if we have made liquidating distributions in full to all holders of preferred stock, we will distribute our remaining assets among the holders of any other classes or series of capital stock ranking junior to the preferred stock according to their respective rights and preferences and, in each case, according to their respective number of shares. For such purposes, our consolidation or merger with or into any other corporation, trust or entity, or the sale, lease or conveyance of all or substantially all of our property or assets will not be deemed to constitute a liquidation, dissolution or winding up of our affairs.

Redemption. If so provided in the applicable prospectus supplement, the preferred stock will be subject to mandatory redemption or redemption at our option, as a whole or in part, in each case upon the terms, at the times and at the redemption prices set forth in such prospectus supplement.

The prospectus supplement relating to a series of preferred stock that is subject to mandatory redemption will specify the number of shares of preferred stock that shall be redeemed by us in each year commencing after

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a date to be specified, at a redemption price per share to be specified, together with an amount equal to all accrued and unpaid dividends thereon to the date of redemption. Unless the shares have a cumulative dividend, such accrued dividends will not include any accumulation in respect of unpaid dividends for prior dividend periods. We may pay the redemption price in cash or other property, as specified in the applicable prospectus supplement. If the redemption price for preferred stock of any series is payable only from the net proceeds of the issuance of shares of our capital stock, the terms of such preferred stock may provide that, if no such shares of our capital stock shall have been issued or to the extent the net proceeds from any issuance are insufficient to pay in full the aggregate redemption price then due, such preferred stock shall automatically and mandatorily be converted into the applicable shares of our capital stock pursuant to conversion provisions specified in the applicable prospectus supplement. Notwithstanding the foregoing, we will not redeem any preferred stock of a series unless:

- if that series of preferred stock has a cumulative dividend, we have declared and paid or contemporaneously declare and pay or set aside funds to pay full cumulative dividends on the preferred stock for all past dividend periods and the then current dividend period; or
- if such series of preferred stock does not have a cumulative dividend, we have declared and paid or contemporaneously declare and pay or set aside funds to pay full dividends for the then current dividend period.

In addition, we will not acquire any preferred stock of a series unless:

- if that series of preferred stock has a cumulative dividend, we have declared and paid or contemporaneously declare and pay or set aside funds to pay full cumulative dividends on all outstanding shares of such series of preferred stock for all past dividend periods and the then current dividend period; or
- if that series of preferred stock does not have a cumulative dividend, we have declared and paid or contemporaneously declare and pay or set aside funds to pay full dividends on the preferred stock of such series for the then current dividend period.

However, at any time we may purchase or acquire preferred stock of that series (1) pursuant to a purchase or exchange offer made on the same terms to holders of all outstanding preferred stock of such series or (2) by conversion into or exchange for shares of our capital stock ranking junior to the preferred stock of such series as to dividends and upon liquidation.

If fewer than all of the outstanding shares of preferred stock of any series are to be redeemed, we will determine the number of shares that may be redeemed pro rata from the holders of record of such shares in proportion to the number of such shares held or for which redemption is requested by such holder or by any other equitable manner that we determine. Such determination will reflect adjustments to avoid redemption of fractional shares.

Unless otherwise specified in the prospectus supplement, we will mail notice of redemption at least 30 days but not more than 60 days before the redemption date to each holder of record of preferred stock to be redeemed at the address shown on our stock transfer books. Each notice shall state:

- the redemption date;
- the number of shares and series of preferred stock to be redeemed;
- the redemption price;
- the place or places where certificates for such preferred stock are to be surrendered for payment of the redemption price;
- that dividends on the shares to be redeemed will cease to accrue on such redemption date;

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- the date on which the holder's conversion rights, if any, as to such shares shall terminate; and
- the specific number of shares to be redeemed from each such holder if fewer than all the shares of any series are to be redeemed.

If notice of redemption has been given and we have set aside the funds necessary for such redemption in trust for the benefit of the holders of any shares called for redemption, then from and after the redemption date, dividends will cease to accrue on such shares, and all rights of the holders of such shares will terminate, except the right to receive the redemption price.

Voting Rights. Holders of preferred stock will not have any voting rights, except as required by law or as indicated in the applicable prospectus supplement.

Unless otherwise provided for under the terms of any series of preferred stock, no consent or vote of the holders of shares of preferred stock or any series thereof shall be required for any amendment to our certificate of incorporation that would increase the number of authorized shares of preferred stock or the number of authorized shares of any series thereof or decrease the number of authorized shares of preferred stock or the number of authorized shares of any series thereof (but not below the number of authorized shares of preferred stock or such series, as the case may be, then outstanding).

Conversion Rights. The terms and conditions, if any, upon which any series of preferred stock is convertible into our common stock will be set forth in the applicable prospectus supplement relating thereto. Such terms will include the number of shares of common stock into which the shares of preferred stock are convertible, the conversion price, rate or manner of calculation thereof, the conversion period, provisions as to whether conversion will be at our option or at the option of the holders of the preferred stock, the events requiring an adjustment of the conversion price and provisions affecting conversion in the event of the redemption.

Transfer Agent and Registrar. The transfer agent and registrar for the preferred stock will be set forth in the applicable prospectus supplement.

Delaware Anti-Takeover Law and Certain Charter and Bylaw Provisions

Delaware Law

We are subject to Section 203 of the Delaware General Corporation Law, or DGCL. Subject to certain exceptions, Section 203 prevents a publicly held Delaware corporation from engaging in a "business combination" with any "interested stockholder" for three years following the date that the person became an interested stockholder, unless either the interested stockholder attained such status with the approval of our board of directors, the business combination is approved by our board of directors and stockholders in a prescribed manner or the interested stockholder acquired at least 85% of our outstanding voting stock in the transaction in which it became an interested stockholder. A "business combination" includes, among other things, a merger or consolidation involving us and the "interested stockholder" and the sale of more than 10% of our assets. In general, an "interested stockholder" is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person.

Staggered Board; Removal of Directors

Our certificate of incorporation and our bylaws divide our board of directors into three classes with staggered three-year terms. In addition, our certificate of incorporation and our bylaws provide that directors may be removed only for cause and only by the affirmative vote of the holders of at least 75% of our shares of capital stock present in person or by proxy and entitled to vote in an election of directors or class of directors. Under our certificate of incorporation and our bylaws, any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in

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office. Furthermore, our certificate of incorporation provides that the authorized number of directors may be changed only by the resolution of our board of directors. The classification of our board of directors and the limitations on the ability of our stockholders to remove directors, change the authorized number of directors and fill vacancies could make it more difficult for a third party to acquire, or discourage a third party from seeking to acquire, control of our company.

Stockholder Action; Special Meeting of Stockholders; Advance Notice Requirements for Stockholder Proposals and Director Nominations

Our certificate of incorporation and our bylaws provide that any action required or permitted to be taken by our stockholders at an annual meeting or special meeting of stockholders may only be taken if it is properly brought before such meeting and may not be taken by written action in lieu of a meeting. Our certificate of incorporation and our bylaws also provide that, except as otherwise required by law, special meetings of the stockholders can only be called by our board of directors. In addition, our bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of stockholders, including proposed nominations of candidates for election to our board of directors. Stockholders at an annual meeting may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of our board of directors, or by a stockholder of record on the record date for the meeting who is entitled to vote at the meeting and who has delivered timely written notice in proper form to our secretary of the stockholder's intention to bring such business before the meeting. These provisions could have the effect of delaying until the next stockholder meeting stockholder actions that are favored by the holders of a majority of our outstanding voting securities. These provisions also could discourage a third party from making a tender offer for our common stock because even if the third party acquired a majority of our outstanding voting stock, it would be able to take action as a stockholder, such as electing new directors or approving a merger, only at a duly called stockholders meeting and not by written consent.

Super-Majority Voting

The DGCL provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or bylaws unless a corporation's certificate of incorporation or bylaws, as the case may be, requires a greater percentage. Our bylaws may be amended or repealed by a majority vote of our board of directors or the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in any annual election of directors. In addition, the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in any election of directors is required to amend or repeal or to adopt any provisions inconsistent with any of the provisions of our certificate of incorporation described above.

Exclusive Forum Selection

Our certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if the Court of Chancery of the State of Delaware does not have jurisdiction, the federal district court for the District of Delaware) shall be the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, other employees or stockholders to our company or our stockholders, (3) any action asserting a claim arising pursuant to any provision of the DGCL or as to which the DGCL confers jurisdiction on the Court of Chancery of the State of Delaware or (4) any action asserting a claim arising pursuant to any provision of our certificate of incorporation or bylaws (in each case, as they may be amended from time to time) or governed by the internal affairs doctrine. This exclusive forum provision will not apply to actions arising under the Securities Act or the Exchange Act. Although our certificate of incorporation contains the choice of forum provision described above, it is possible that a court could rule that such a provision is inapplicable for a particular claim or action or that such provision is unenforceable.

Registration Rights

Investors' Rights Agreement

We have entered into an amended and restated investors' rights agreement dated as of August 24, 2018, or the investors' rights agreement, with certain holders of our common stock who have the right to require us to register such shares of common stock under the Securities Act under specified circumstances. We refer to the shares with these registration rights as registrable securities. After registration pursuant to these rights, the registrable securities will become freely tradable without restriction under the Securities Act.

Demand and Form S-3 Registration Rights

Subject to specified limitations set forth in the investors' rights agreement, at any time, the holders of at least 40% of the then outstanding registrable securities may demand that we register at least 40% of the registrable securities then outstanding under the Securities Act for purposes of a public offering having an aggregate offering price to the public of not less than \$5.0 million. We are not obligated to file a registration statement pursuant to this provision on more than two occasions.

In addition, subject to specified limitations set forth in the investors' rights agreement, at any time after we become eligible to file a registration statement on Form S-3, the holders of at least 25% of the then outstanding registrable securities may request that we register their registrable securities on Form S-3 for purposes of a public offering for which the reasonably anticipated aggregate offering price to the public would be at least \$3.0 million. We are not obligated to file a registration statement pursuant to this provision on more than two occasions in any 12-month period.

Incidental Registration Rights

If, at any time, we propose to register for our own account (including, for this purpose, a registration effected by us for stockholders who are not holders of registrable securities under the investors' rights agreement) any of our securities under the Securities Act, the holders of registrable securities will be entitled to notice of the registration and, subject to specified exceptions, have the right to require us to use our commercially reasonable efforts to register all or a portion of the registrable securities then held by them in that registration.

In the event that any registration in which the holders of registrable securities participate pursuant to our investors' rights agreement is an underwritten public offering, we have agreed to enter into an underwriting agreement in usual and customary form and use our reasonable best efforts to facilitate such offering.

Expenses

Pursuant to the investors' rights agreement, we are required to pay all registration expenses, including all registration and filing fees, exchange listing fees, printing expenses, fees and expenses of one counsel selected by the selling stockholders to represent the selling stockholders, state Blue Sky fees and expenses, and the expense of any special audits incident to or required by any such registration, but excluding underwriting discounts, selling commissions, stock transfer taxes applicable to the sale any registrable securities and the fees and expenses of the selling stockholders' own counsel (other than the counsel selected to represent all selling stockholders). If a registration is withdrawn at the request of the stockholders initiating the registration, then the stockholders will bear the expenses of the registration.

The investors' rights agreement contains customary cross-indemnification provisions, pursuant to which we are obligated to indemnify the selling stockholders in the event of material misstatements or omissions in the registration statement attributable to us or any violation or alleged violation whether by action or inaction by us under the Securities Act, the Exchange Act, any state securities or Blue Sky law or any rule or regulation promulgated under the Securities Act, the Exchange Act or any state securities or Blue Sky law in connection with such registration statement or the qualification or compliance of the offering, and they are obligated to indemnify us for material misstatements or omissions in the registration statement attributable to them.

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Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A.

Nasdaq Global Market

Our common stock is listed on the Nasdaq Global Market under the symbol “FULC.”

DESCRIPTION OF DEPOSITARY SHARES

General

We may, at our option, elect to offer fractional shares of preferred stock, which we call depositary shares, rather than full shares of preferred stock. If we do, we will issue to the public receipts, called depositary receipts, for depositary shares, each of which will represent a fraction, to be described in the applicable prospectus supplement, of a share of a particular series of preferred stock. Unless otherwise provided in the prospectus supplement, each owner of a depositary share will be entitled, in proportion to the applicable fractional interest in a share of preferred stock represented by the depositary share, to all the rights and preferences of the preferred stock represented by the depositary share. Those rights include dividend, voting, redemption, conversion and liquidation rights.

The shares of preferred stock underlying the depositary shares will be deposited with a bank or trust company selected by us to act as depositary under a deposit agreement between us, the depositary and the holders of the depositary receipts. The depositary will be the transfer agent, registrar and dividend disbursing agent for the depositary shares.

The depositary shares will be evidenced by depositary receipts issued pursuant to the deposit agreement. Holders of depositary receipts agree to be bound by the deposit agreement, which requires holders to take certain actions such as filing proof of residence and paying certain charges.

The summary of terms of the depositary shares contained in this prospectus is not a complete description of the terms of the depositary shares. You should refer to the form of the deposit agreement, our certificate of incorporation and the certificate of designation for the applicable series of preferred stock that are, or will be, filed with the SEC.

Dividends and Other Distributions

The depositary will distribute all cash dividends or other cash distributions, if any, received in respect of the preferred stock underlying the depositary shares to the record holders of depositary shares in proportion to the numbers of depositary shares owned by those holders on the relevant record date. The relevant record date for depositary shares will be the same date as the record date for the underlying preferred stock.

If there is a distribution other than in cash, the depositary will distribute property (including securities) received by it to the record holders of depositary shares, unless the depositary determines that it is not feasible to make the distribution. If this occurs, the depositary may, with our approval, adopt another method for the distribution, including selling the property and distributing the net proceeds from the sale to the holders.

Liquidation Preference

If a series of preferred stock underlying the depositary shares has a liquidation preference, in the event of the voluntary or involuntary liquidation, dissolution or winding up of us, holders of depositary shares will be entitled to receive the fraction of the liquidation preference accorded each share of the applicable series of preferred stock, as set forth in the applicable prospectus supplement.

Withdrawal of Stock

Unless the related depositary shares have been previously called for redemption, upon surrender of the depositary receipts at the office of the depositary, the holder of the depositary shares will be entitled to delivery, at the office of the depositary to or upon his or her order, of the number of whole shares of the preferred stock and any money or other property represented by the depositary shares. If the depositary receipts delivered by the

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holder evidence a number of depositary shares in excess of the number of depositary shares representing the number of whole shares of preferred stock to be withdrawn, the depositary will deliver to the holder at the same time a new depositary receipt evidencing the excess number of depositary shares. In no event will the depositary deliver fractional shares of preferred stock upon surrender of depositary receipts. Holders of preferred stock thus withdrawn may not thereafter deposit those shares under the deposit agreement or receive depositary receipts evidencing depositary shares therefor.

Redemption of Depositary Shares

Whenever we redeem shares of preferred stock held by the depositary, the depositary will redeem as of the same redemption date the number of depositary shares representing shares of the preferred stock so redeemed, so long as we have paid in full to the depositary the redemption price of the preferred stock to be redeemed plus an amount equal to any accumulated and unpaid dividends on the preferred stock to the date fixed for redemption. The redemption price per depositary share will be equal to the redemption price and any other amounts per share payable on the preferred stock multiplied by the fraction of a share of preferred stock represented by one depositary share. If less than all the depositary shares are to be redeemed, the depositary shares to be redeemed will be selected by lot or pro rata or by any other equitable method as may be determined by the depositary.

After the date fixed for redemption, depositary shares called for redemption will no longer be deemed to be outstanding and all rights of the holders of depositary shares will cease, except the right to receive the monies payable upon redemption and any money or other property to which the holders of the depositary shares were entitled upon redemption upon surrender to the depositary of the depositary receipts evidencing the depositary shares.

Voting the Preferred Stock

Upon receipt of notice of any meeting at which the holders of the preferred stock are entitled to vote, the depositary will mail the information contained in the notice of meeting to the record holders of the depositary receipts relating to that preferred stock. The record date for the depositary receipts relating to the preferred stock will be the same date as the record date for the preferred stock. Each record holder of the depositary shares on the record date will be entitled to instruct the depositary as to the exercise of the voting rights pertaining to the number of shares of preferred stock represented by that holder's depositary shares. The depositary will endeavor, insofar as practicable, to vote the number of shares of preferred stock represented by the depositary shares in accordance with those instructions, and we will agree to take all action that may be deemed necessary by the depositary in order to enable the depositary to do so. The depositary will not vote any shares of preferred stock except to the extent it receives specific instructions from the holders of depositary shares representing that number of shares of preferred stock.

Charges of Depositary

We will pay all transfer and other taxes and governmental charges arising solely from the existence of the depositary arrangements. We will pay charges of the depositary in connection with the initial deposit of the preferred stock and any redemption of the preferred stock. Holders of depositary receipts will pay transfer, income and other taxes and governmental charges and such other charges (including those in connection with the receipt and distribution of dividends, the sale or exercise of rights, the withdrawal of the preferred stock and the transferring, splitting or grouping of depositary receipts) as are expressly provided in the deposit agreement to be for their accounts. If these charges have not been paid by the holders of depositary receipts, the depositary may refuse to transfer depositary shares, withhold dividends and distributions and sell the depositary shares evidenced by the depositary receipt.

Amendment and Termination of the Deposit Agreement

The form of depositary receipt evidencing the depositary shares and any provision of the deposit agreement may be amended by agreement between us and the depositary. However, any amendment that materially and

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adversely alters the rights of the holders of depositary shares, other than fee changes, will not be effective unless the amendment has been approved by the holders of a majority of the outstanding depositary shares. The deposit agreement may be terminated by the depositary or us only if:

- all outstanding depositary shares have been redeemed; or
- there has been a final distribution of the preferred stock in connection with our dissolution and such distribution has been made to all the holders of depositary shares.

Resignation and Removal of Depositary

The depositary may resign at any time by delivering to us notice of its election to do so, and we may remove the depositary at any time. Any resignation or removal of the depositary will take effect upon our appointment of a successor depositary and its acceptance of such appointment. The successor depositary must be appointed within 60 days after delivery of the notice of resignation or removal and must be a bank or trust company having its principal office in the United States and having the requisite combined capital and surplus as set forth in the applicable agreement.

Notices

The depositary will forward to holders of depositary receipts all notices, reports and other communications, including proxy solicitation materials received from us, that are delivered to the depositary and that we are required to furnish to the holders of the preferred stock. In addition, the depositary will make available for inspection by holders of depositary receipts at the principal office of the depositary, and at such other places as it may from time to time deem advisable, any reports and communications we deliver to the depositary as the holder of preferred stock.

Limitation of Liability

Neither we nor the depositary will be liable if either we or it is prevented or delayed by law or any circumstance beyond its control in performing its obligations. Our obligations and those of the depositary will be limited to performance in good faith of our and their duties thereunder. We and the depositary will not be obligated to prosecute or defend any legal proceeding in respect of any depositary shares or preferred stock unless satisfactory indemnity is furnished. We and the depositary may rely upon written advice of counsel or accountants, on information provided by persons presenting preferred stock for deposit, holders of depositary receipts or other persons believed to be competent to give such information and on documents believed to be genuine and to have been signed or presented by the proper party or parties.

DESCRIPTION OF UNITS

We may issue units comprised of one or more of the other securities that may be offered under this prospectus, in any combination. The following, together with the additional information we may include in any applicable prospectus supplement, summarizes the material terms and provisions of the units that we may offer under this prospectus. While the terms summarized below will apply generally to any units we may offer, we will describe the particular terms of any series of units in more detail in the applicable prospectus supplement. If we indicate in the prospectus supplement, the terms of any units offered under that prospectus supplement may differ from the terms described below. Specific unit agreements will contain additional important terms and provisions and will be incorporated by reference as an exhibit to the registration statement that includes this prospectus.

Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately at any time, or at any time before a specified date.

We will describe in the applicable prospectus supplement the terms of the series of units being offered, including:

- the material terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any material provisions relating to the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units; and
- any material provisions of the governing unit agreement that differ from those described above.

We may issue units in such amounts and in such numbers of distinct series as we determine.

The provisions described in this section, as well as those described under “Description of Debt Securities,” “Description of Capital Stock,” “Description of Depositary Shares” and “Description of Warrants” will apply to each unit, as applicable, and to any debt securities, common stock, preferred stock, depositary share or warrant included in each unit, as applicable.

Unit Agent

The name and address of the unit agent for any units we offer will be set forth in the applicable prospectus supplement.

Enforceability of Rights by Holders of Units

Each unit agent will act solely as our agent under the applicable unit agreement and will not assume any obligation or relationship of agency or trust with any holder of any unit. A single bank or trust company may act as unit agent for more than one series of units. A unit agent will have no duty or responsibility in case of any default by us under the applicable unit agreement or unit, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a unit may, without the consent of the related unit agent or the holder of any other unit, enforce by appropriate legal action its rights as holder under any security included in the unit.

DESCRIPTION OF WARRANTS

We may issue warrants to purchase common stock, preferred stock, depositary shares or debt securities. We may offer warrants separately or together with one or more additional warrants, common stock, preferred stock, depositary shares or debt securities, or any combination of those securities in the form of units, as described in the applicable prospectus supplement. If we issue warrants as part of a unit, the accompanying prospectus supplement will specify whether those warrants may be separated from the other securities in the unit prior to the expiration date of the warrants. The applicable prospectus supplement will also describe the following terms of any warrants:

- the specific designation and aggregate number of, and the offering price at which we will issue, the warrants;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if you may not continuously exercise the warrants throughout that period, the specific date or dates on which you may exercise the warrants;
- whether the warrants are to be sold separately or with other securities as parts of units;
- whether the warrants will be issued in definitive or global form or in any combination of these forms, although, in any case, the form of a warrant included in a unit will correspond to the form of the unit and of any security included in that unit;
- any applicable material U.S. federal income tax consequences;
- the identity of the warrant agent for the warrants and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;
- the proposed listing, if any, of the warrants or any securities purchasable upon exercise of the warrants on any securities exchange;
- the designation and terms of any equity securities purchasable upon exercise of the warrants;
- the designation, aggregate principal amount, currency and terms of any debt securities that may be purchased upon exercise of the warrants;
- if applicable, the designation and terms of the preferred stock or depositary shares with which the warrants are issued and the number of warrants issued with each security;
- if applicable, the date from and after which any warrants issued as part of a unit and the related debt securities, preferred stock, depositary shares or common stock will be separately transferable;
- the number of shares of common stock, preferred stock or depositary shares purchasable upon exercise of a warrant and the price at which those shares may be purchased;
- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;
- information with respect to book-entry procedures, if any;
- the anti-dilution provisions of, and other provisions for changes to or adjustment in the exercise price of, the warrants, if any;
- any redemption or call provisions; and
- any additional terms of the warrants, including terms, procedures and limitations relating to the exchange or exercise of the warrants.

FORMS OF SECURITIES

Each debt security, depositary share, unit and warrant will be represented either by a certificate issued in definitive form to a particular investor or by one or more global securities representing the entire issuance of securities. Unless the applicable prospectus supplement provides otherwise, certificated securities in definitive form and global securities will be issued in registered form. Definitive securities name you or your nominee as the owner of the security, and in order to transfer or exchange these securities or to receive payments other than interest or other interim payments, you or your nominee must physically deliver the securities to the trustee, registrar, paying agent or other agent, as applicable. Global securities name a depositary or its nominee as the owner of the debt securities, depositary shares, units or warrants represented by these global securities. The depositary maintains a computerized system that will reflect each investor's beneficial ownership of the securities through an account maintained by the investor with its broker/dealer, bank, trust company or other representative, as we explain more fully below.

Global Securities

We may issue the debt securities, depositary shares, units and warrants in the form of one or more fully registered global securities that will be deposited with a depositary or its nominee identified in the applicable prospectus supplement and registered in the name of that depositary or nominee. In those cases, one or more global securities will be issued in a denomination or aggregate denominations equal to the portion of the aggregate principal or face amount of the securities to be represented by global securities. Unless and until it is exchanged in whole for securities in definitive registered form, a global security may not be transferred except as a whole by and among the depositary for the global security, the nominees of the depositary or any successors of the depositary or those nominees.

If not described below, any specific terms of the depositary arrangement with respect to any securities to be represented by a global security will be described in the prospectus supplement relating to those securities. We anticipate that the following provisions will apply to all depositary arrangements.

Ownership of beneficial interests in a global security will be limited to persons, called participants, that have accounts with the depositary or persons that may hold interests through participants. Upon the issuance of a global security, the depositary will credit, on its book-entry registration and transfer system, the participants' accounts with the respective principal or face amounts of the securities beneficially owned by the participants. Any dealers, underwriters or agents participating in the distribution of the securities will designate the accounts to be credited. Ownership of beneficial interests in a global security will be shown on, and the transfer of ownership interests will be effected only through, records maintained by the depositary, with respect to interests of participants, and on the records of participants, with respect to interests of persons holding through participants. The laws of some states may require that some purchasers of securities take physical delivery of these securities in definitive form. These laws may impair your ability to own, transfer or pledge beneficial interests in global securities.

So long as the depositary, or its nominee, is the registered owner of a global security, that depositary or its nominee, as the case may be, will be considered the sole owner or holder of the securities represented by the global security for all purposes under the applicable indenture, deposit agreement, warrant agreement or unit agreement. Except as described below, owners of beneficial interests in a global security will not be entitled to have the securities represented by the global security registered in their names, will not receive or be entitled to receive physical delivery of the securities in definitive form and will not be considered the owners or holders of the securities under the applicable indenture, deposit agreement, unit agreement or warrant agreement. Accordingly, each person owning a beneficial interest in a global security must rely on the procedures of the depositary for that global security and, if that person is not a participant, on the procedures of the participant through which the person owns its interest, to exercise any rights of a holder under the applicable indenture, deposit agreement, unit agreement or warrant agreement. We understand that under existing industry practices, if

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we request any action of holders or if an owner of a beneficial interest in a global security desires to give or take any action that a holder is entitled to give or take under the applicable indenture, deposit agreement, unit agreement or warrant agreement, the depository for the global security would authorize the participants holding the relevant beneficial interests to give or take that action, and the participants would authorize beneficial owners owning through them to give or take that action or would otherwise act upon the instructions of beneficial owners holding through them.

Principal, premium, if any, and interest payments on debt securities, and any payments to holders with respect to depository shares, warrants or units, represented by a global security registered in the name of a depository or its nominee will be made to the depository or its nominee, as the case may be, as the registered owner of the global security. None of us, or any trustee, warrant agent, unit agent or other agent of ours, or any agent of any trustee, warrant agent or unit agent will have any responsibility or liability for any aspect of the records relating to payments made on account of beneficial ownership interests in the global security or for maintaining, supervising or reviewing any records relating to those beneficial ownership interests.

We expect that the depository for any of the securities represented by a global security, upon receipt of any payment to holders of principal, premium, interest or other distribution of underlying securities or other property on that registered global security, will immediately credit participants' accounts in amounts proportionate to their respective beneficial interests in that global security as shown on the records of the depository. We also expect that payments by participants to owners of beneficial interests in a global security held through participants will be governed by standing customer instructions and customary practices, as is now the case with the securities held for the accounts of customers or registered in "street name," and will be the responsibility of those participants.

If the depository for any of the securities represented by a global security is at any time unwilling or unable to continue as depository or ceases to be a clearing agency registered under the Exchange Act, and a successor depository registered as a clearing agency under the Exchange Act is not appointed by us within 90 days, we will issue securities in definitive form in exchange for the global security that had been held by the depository. Any securities issued in definitive form in exchange for a global security will be registered in the name or names that the depository gives to the relevant trustee, warrant agent, unit agent or other relevant agent of ours or theirs. It is expected that the depository's instructions will be based upon directions received by the depository from participants with respect to ownership of beneficial interests in the global security that had been held by the depository.

PLAN OF DISTRIBUTION

We may sell securities:

- to or through underwriters;
- to or through brokers or dealers;
- through agents;
- directly to one or more purchasers in negotiated sales or competitively bid transactions;
- through a block trade in which the broker or dealer engaged to handle the block trade will attempt to sell the securities as agent, but may position and resell a portion of the block as principal to facilitate the transaction; or
- through a combination of any of these methods of sale.

In addition, we may issue the securities as a dividend or distribution or in a subscription rights offering to our existing security holders. This prospectus may be used in connection with any offering of our securities through any of these methods or other methods described in the applicable prospectus supplement.

We may directly solicit offers to purchase securities, or agents may be designated to solicit such offers. We will, in the prospectus supplement relating to such offering, name any agent that could be viewed as an underwriter under the Securities Act, and describe any commissions that we must pay. Any such agent will be acting on a best efforts basis for the period of its appointment or, if indicated in the applicable prospectus supplement, on a firm commitment basis.

The distribution of the securities may be effected from time to time in one or more transactions:

- at a fixed price, or prices, which may be changed from time to time;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

Each prospectus supplement will describe the method of distribution of the securities and any applicable restrictions.

The prospectus supplement with respect to the securities of a particular series will describe the terms of the offering of the securities, including the following:

- the name of the agent or any underwriters;
- the public offering or purchase price and the proceeds we will receive from the sale of the securities;
- any discounts and commissions to be allowed or re-allowed or paid to the agent or underwriters;
- all other items constituting underwriting compensation;
- any discounts and commissions to be allowed or re-allowed or paid to dealers; and
- any exchanges on which the securities will be listed.

If any underwriters or agents are utilized in the sale of the securities in respect of which this prospectus is delivered, we will enter into an underwriting agreement or other agreement with them at the time of sale to them, and we will set forth in the prospectus supplement relating to such offering the names of the underwriters or agents and the terms of the related agreement with them.

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If a dealer is utilized in the sale of the securities in respect of which this prospectus is delivered, we will sell such securities to the dealer, as principal. The dealer may then resell such securities to the public at varying prices to be determined by such dealer at the time of resale.

If we offer securities in a subscription rights offering to our existing security holders, we may enter into a standby underwriting agreement with dealers, acting as standby underwriters. We may pay the standby underwriters a commitment fee for the securities they commit to purchase on a standby basis. If we do not enter into a standby underwriting arrangement, we may retain a dealer-manager to manage a subscription rights offering for us.

Remarketing firms, agents, underwriters, dealers and other persons may be entitled under agreements which they may enter into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, and may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

If so indicated in the applicable prospectus supplement, we will authorize underwriters or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and delivery on the date stated in the prospectus supplement. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not be less nor more than, the respective amounts stated in the prospectus supplement. Institutions with whom the contracts, when authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will not be subject to any conditions except that:

- the purchase by an institution of the securities covered under that contract shall not at the time of delivery be prohibited under the laws of the jurisdiction to which that institution is subject; and
- if the securities are also being sold to underwriters acting as principals for their own account, the underwriters shall have purchased such securities not sold for delayed delivery. The underwriters and other persons acting as our agents will not have any responsibility in respect of the validity or performance of delayed delivery contracts.

Certain agents, underwriters and dealers, and their associates and affiliates may be customers of, have borrowing relationships with, engage in other transactions with, and/or perform services, including investment banking services, for us or one or more of our respective affiliates in the ordinary course of business.

In order to facilitate the offering of the securities, any underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the securities or any other securities the prices of which may be used to determine payments on such securities. Specifically, any underwriters may overallocate in connection with the offering, creating a short position for their own accounts. In addition, to cover overallocations or to stabilize the price of the securities or of any such other securities, the underwriters may bid for, and purchase, the securities or any such other securities in the open market. Finally, in any offering of the securities through a syndicate of underwriters, the underwriting syndicate may reclaim selling concessions allowed to an underwriter or a dealer for distributing the securities in the offering if the syndicate repurchases previously distributed securities in transactions to cover syndicate short positions, in stabilization transactions or otherwise. Any of these activities may stabilize or maintain the market price of the securities above independent market levels. Any such underwriters are not required to engage in these activities and may end any of these activities at any time.

Under Rule 15c6-1 of the Exchange Act, trades in the secondary market generally are required to settle in two business days, unless the parties to any such trade expressly agree otherwise or the securities are sold by us to an underwriter in a firm commitment underwritten offering. The applicable prospectus supplement may provide that the original issue date for your securities may be more than two scheduled business days after the

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trade date for your securities. Accordingly, in such a case, if you wish to trade securities on any date prior to the second business day before the original issue date for your securities, you will be required, by virtue of the fact that your securities initially are expected to settle in more than two scheduled business days after the trade date for your securities, to make alternative settlement arrangements to prevent a failed settlement.

The securities may be new issues of securities and may have no established trading market. The securities may or may not be listed on a national securities exchange. We can make no assurance as to the liquidity of or the existence of trading markets for any of the securities.

LEGAL MATTERS

Unless the applicable prospectus supplement indicates otherwise, the validity of the securities in respect of which this prospectus is being delivered will be passed upon by Wilmer Cutler Pickering Hale and Dorr LLP.

EXPERTS

The consolidated financial statements of Fulcrum Therapeutics, Inc. appearing in Fulcrum Therapeutics, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2019, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

