

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549**

**FORM S-1
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933**

FULCRUM THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

2834
(Primary Standard Industrial
Classification Code Number)

47-4839948
(I.R.S. Employer
Identification Number)

26 Landsdowne Street
Cambridge, Massachusetts 02139
(617) 651-8851

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Robert J. Gould, Ph.D.
President and Chief Executive Officer
Fulcrum Therapeutics, Inc.
26 Landsdowne Street
Cambridge, Massachusetts 02139
(617) 651-8851

(Name, address, including zip code, and telephone number, including area code, of agent for service)

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Chief Operating Officer
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26 Landsdowne Street
Cambridge, Massachusetts 02139
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Approximate date of commencement of proposed sale to the public: As soon as practicable after this Registration Statement is declared effective.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box.

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

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

Large accelerated filer
Non-accelerated filer

Accelerated filer
Smaller reporting company
Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act.

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to Be Registered	Amount to be Registered(1)(2)	Proposed Maximum Offering Price Per Share(3)	Proposed Maximum Aggregate Offering Price(3)	Amount of Registration Fee(3)
Common stock, par value \$0.001 per share	4,029,411	\$16.77	\$67,573,223	\$8,771

(1) The shares will be offered for resale by selling stockholders.

(2) Pursuant to Rule 416 under the Securities Act of 1933, as amended, this registration statement also covers any additional number of shares of common stock issuable upon stock splits, stock dividends or other distribution, recapitalization or similar events with respect to the shares of common stock being registered pursuant to this registration statement.

(3) Estimated solely for purposes of calculating the registration fee pursuant to Rule 457(c) under the Securities Act of 1933, as amended, and based on the average of the high and low sales price per share of the registrant's common stock on the Nasdaq Global Market on June 15, 2020.

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

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

SUBJECT TO COMPLETION, DATED June 22, 2020

4,029,411 Shares



Common Stock

This prospectus relates to the resale, from time to time, of up to 4,029,411 shares of our common stock by the selling stockholders (which term, as used in this prospectus, includes pledgees, donees, transferees or other successors-in-interest) identified in this prospectus. The selling stockholders acquired the shares of our common stock in our June 2020 private placement.

We are not selling any securities under this prospectus and we will not receive any proceeds from the sale of the shares.

We have agreed to bear all of the expenses incurred in connection with the registration of these shares. The selling stockholders will pay or assume discounts, commissions, fees of underwriters, selling brokers or dealer managers and similar expenses, if any, incurred for the sale of shares of our common stock.

The selling stockholders identified in this prospectus may offer the shares from time to time through public or private transactions at prevailing market prices, at prices related to prevailing market prices or at privately negotiated prices. For additional information on the methods of sale that may be used by the selling stockholders, see the section entitled "Plan of Distribution" on page 17. For a list of the selling stockholders, see the section entitled "Selling Stockholders" on page 14.

We may amend or supplement this prospectus from time to time by filing amendments or supplements as required. You should read the entire prospectus and any amendments or supplements carefully before you make your investment decision.

Our common stock is listed on the Nasdaq Global Market ("Nasdaq") under the symbol "FULC." On June 19, 2020, the closing sale price of our common stock as reported on Nasdaq was \$19.56. You are urged to obtain current market quotations for the common stock.

We are an "emerging growth company" and a "smaller reporting company" under applicable Securities and Exchange Commission rules and, as such, have elected to comply with certain reduced public company disclosure requirements for this prospectus and future filings. See "Prospectus Summary—Implications of Being an Emerging Growth Company and a Smaller Reporting Company."

Our business and investment in our common stock involve significant risks. These risks are described in the section titled "[Risk Factors](#)" beginning on page 5 of this prospectus.

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

The date of this prospectus is _____, 2020

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You should rely only on the information contained or incorporated by reference in this prospectus. We have not authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. This prospectus may only be used where it is legal to offer and sell shares of our common stock. If it is against the law in any jurisdiction to make an offer to sell these shares, or to solicit an offer from someone to buy these shares, then this prospectus does not apply to any person in that jurisdiction, and no offer or solicitation is made by this prospectus to any such person. You should assume that the information appearing in this prospectus is accurate only as of the date on the front cover of this prospectus, regardless of the time of delivery of this prospectus or of any sale of common stock. Our business, financial condition, results of operations and prospects may have changed since such date.

PROSPECTUS SUMMARY

This summary highlights, and is qualified in its entirety by, the more detailed information included elsewhere in this prospectus or incorporated by reference herein. This summary does not contain all of the information that may be important to you. You should read and carefully consider the entire prospectus, especially the “Risk Factors” section of this prospectus, before deciding to invest in our common stock. Unless the context otherwise requires, we use the terms “company,” “we,” “us” and “our” in this prospectus to refer to Fulcrum Therapeutics, Inc. and our subsidiary.

Overview

We are a clinical-stage biopharmaceutical company focused on improving the lives of patients with genetically defined rare diseases in areas of high unmet medical need. We have developed a proprietary product engine that we employ to systematically identify and validate cellular drug targets that can potentially modulate gene expression to treat the known root cause of genetically defined diseases. We are using our product engine to identify targets that can be drugged by small molecules regardless of the particular underlying mechanism of gene mis-expression. We have identified drug targets to treat the root causes of facioscapulohumeral muscular dystrophy, or FSHD, and certain hemoglobinopathies, namely sickle cell disease, or SCD, and β -thalassemia. In August 2019, we initiated a Phase 2b clinical trial, known as ReDUX4, and a Phase 2 open label clinical trial of losmapimod, our product candidate for FSHD, to evaluate the efficacy and safety of losmapimod in addressing the underlying cause of FSHD. We plan to submit one or more regulatory filings for FTX-6058, our product candidate for certain hemoglobinopathies, in the second half of 2020. FTX-6058 is a novel upregulator of fetal hemoglobin.

On June 10, 2020, we announced plans to evaluate losmapimod as a potential treatment for patients with COVID-19. Following pre-IND consultation via the Coronavirus Treatment Acceleration Program (CTAP), we have submitted an investigational new drug application, or IND, with the U.S. Food and Drug Administration to support initiation of a randomized, placebo-controlled, Phase 3 clinical trial in hospitalized patients in the United States.

Our Corporate Information

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

Implications of Being an Emerging Growth Company 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 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.

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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 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 by selling stockholders	4,029,411 shares
Use of proceeds	We will not receive any proceeds from the sale of shares in this offering.
Risk factors	You should read the “Risk Factors” section included or incorporated by reference in this prospectus for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.
Nasdaq Global Market symbol	“FULC”

DESCRIPTION OF PRIVATE PLACEMENT WITH THE SELLING STOCKHOLDERS

On June 9, 2020, we entered into a securities purchase agreement for a private placement with the selling stockholders whereby, on June 9, 2020, we issued and sold 4,029,411 shares of our common stock at a price of \$17.00 per share for gross proceeds of approximately \$68.5 million. For a detailed description of the transactions contemplated by the securities purchase agreement with the selling stockholders and the securities issued pursuant thereto, see the section captioned "Selling Stockholders" in this prospectus. We filed the registration statement on Form S-1, of which this prospectus forms a part, to fulfill our contractual obligations under the registration rights agreement entered into concurrently with the securities purchase agreement with the selling stockholders to provide for the resale by the selling stockholders of the shares of common stock offered hereby.

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 described in the section captioned “Risk Factors” in our most recent Annual Report on Form 10-K, our most recent Quarterly Report on Form 10-Q and other filings we make with the Securities and Exchange Commission, or SEC, from time to time, which are incorporated by reference herein in their entirety, together with the other information in this prospectus and documents incorporated by reference in this prospectus. The risks described in our most recent Annual Report on Form 10-K, our most recent Quarterly Report on Form 10-Q and the other filings incorporated by reference herein are not the only ones facing our company. Additional risks and uncertainties may also impair our business operations. If any of the risks described in our most recent Annual Report on Form 10-K, our most recent Quarterly Report on Form 10-Q and the other filings incorporated by reference herein occurs, our business, financial condition, results of operations and future growth prospects could be harmed. In these circumstances, the market price of our common stock could decline, and you may lose all or part of your investment.

In addition to the risk factors incorporated by reference herein, the following risk factor is included:

We may not be successful in our efforts to develop losmapimod for the treatment of patients with COVID-19.

On June 10, 2020, we announced plans to evaluate losmapimod as a potential treatment for patients with COVID-19. Following pre-IND consultation via the Coronavirus Treatment Acceleration Program (CTAP), we have submitted an investigational new drug application, or IND, with the U.S. Food and Drug Administration, or the FDA, to support initiation of a randomized, placebo-controlled, Phase 3 clinical trial in hospitalized patients in the United States.

The initiation of our clinical trial of losmapimod for the treatment of patients with COVID-19 is pending review of our recently filed IND by the FDA. We also need to reach agreement with prospective clinical trial sites and may be delayed in doing so or fail to do so. The timing and success of our clinical trial of losmapimod for the treatment of patients with COVID-19 will depend on our ability to enroll patients in the trial. Many other companies are pursuing the development of product candidates for the treatment of COVID-19, and patient enrollment may be affected by availability of commercially available treatments and other clinical trials of competing product candidates. Patient enrollment may also be affected by other factors, including the incidence of COVID-19 over time and the perceived risks and benefits of the use of losmapimod as a treatment relative to competing treatments. Our inability to enroll a sufficient number of patients could result in significant delays or could require us to abandon the trial and development of losmapimod for the treatment of COVID-19 altogether.

The COVID-19 pandemic may be effectively contained before we can successfully develop losmapimod as a treatment for COVID-19 and recoup our financial investment in the trial through sales of losmapimod. For example, a vaccine may be developed and available in sufficient quantities to contain the spread of the SARS-CoV-2 virus before we are able to complete our planned Phase 3 clinical trial. Our commitment of financial resources and personnel to the development of losmapimod for the treatment of COVID-19 may cause delays in or otherwise negatively impact our other development programs and research and discovery efforts with our product engine.

Additionally, while losmapimod has been previously tested in more than 3,600 subjects, including in clinical trials evaluating the ability of an oral dose of 15 mg twice per day of losmapimod to restore a normal immune response in older patients challenged with a viral antigen, it has not been evaluated as a treatment in the acute infection setting. It is possible that unexpected safety issues, including issues that have not been observed in prior clinical trials of losmapimod, could occur in patients with COVID-19. Any such safety issues could affect our development program for losmapimod for the treatment of FSHD and our ability to obtain marketing approval for losmapimod, including our ability to apply for accelerated approval.

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Given the rapidity of the onset of the COVID-19 pandemic, scientific and medical research on the SARS-CoV-2 virus is ongoing and evolving. We cannot be certain that the preclinical and clinical evidence that we believe suggests that losmapimod may be beneficial to patients with COVID-19 will be established in a clinical trial. Similarly, we cannot be certain that the planned Phase 3 clinical trial will be sufficient to enable us to obtain marketing approval of losmapimod for the treatment of COVID-19, and we may need to conduct additional clinical trials before we are able to apply for marketing approval. Furthermore, the failure of losmapimod to demonstrate safety and efficacy in patients with COVID-19 could negatively impact the perception of us and losmapimod by investors.

In the future, we may seek to make losmapimod available for the treatment of COVID-19 through an Emergency Use Authorization Program, or the FDA or other government body may request that losmapimod is made available through an Emergency Use Authorization. The FDA has the authority to grant an Emergency Use Authorization to allow unapproved medical products to be used in an emergency to diagnose, treat or prevent serious or life-threatening diseases or conditions when there are no adequate, approved and available alternatives. If we are granted an Emergency Use Authorization for losmapimod for the treatment of COVID-19, we would be able to commercialize losmapimod for the treatment of COVID-19 prior to FDA approval of a new drug application, or NDA. However, the FDA may revoke an Emergency Use Authorization where it is determined that the underlying health emergency no longer exists or warrants such authorization, and we cannot predict how long, if ever, an Emergency Use Authorization would remain in place. Such revocation could adversely impact our business in a variety of ways, including if losmapimod for the treatment of COVID-19 is not yet approved by the FDA via an NDA and if we and our manufacturing partners have invested in the supply chain to provide losmapimod for the treatment of COVID-19 under an Emergency Use Authorization.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

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

The forward-looking statements contained in this prospectus and incorporated by reference herein include, among other things, statements about:

- our ongoing Phase 2b and Phase 2 open label clinical trials of losmapimod;
- our planned Phase 1 clinical trial of FTX-6058;
- our planned Phase 3 clinical trial of losmapimod for hospitalized patients with novel coronavirus, or COVID-19, pending review of our recently filed IND by the U.S. Food and Drug Administration;
- 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;
- 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 collaboration with Acceleron Pharma Inc.;
- our ability to identify additional products, product candidates or technologies with significant commercial potential that are consistent with our commercial objectives;
- our estimates regarding expenses, future revenue, timing of any future revenue, capital requirements and needs for additional financing;
- the impact of government laws and regulations;
- our competitive position;
- developments relating to our competitors and our industry;
- our ability to maintain and establish collaborations or obtain additional funding;

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- our expectations regarding the time during which we will be an emerging growth company under the Jumpstart Our Business Startups Act of 2012; and
- other risks and uncertainties, including those listed under the caption “Risk Factors” in our most recent Annual Report on Form 10-K, our most recent Quarterly Report on Form 10-Q, and other filings we make with the SEC.

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 and incorporated by reference herein, particularly in the “Risk Factors” section, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, collaborations, joint ventures or investments we may make or enter into.

You should read this prospectus, 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, whether as a result of new information, future events or otherwise, except as required by applicable law.

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

USE OF PROCEEDS

We are filing the registration statement of which this prospectus is a part to permit holders of the shares of our common stock described in the section entitled "Selling Stockholders" to resell such shares. We are not selling any securities under this prospectus and we will not receive any proceeds from the sale of shares by the selling stockholders.

The selling stockholders will pay any discounts, commissions, fees of underwriters, selling brokers or dealer managers and expenses incurred by the selling stockholders for brokerage, accounting, tax or legal services or any other expenses incurred by the selling stockholders in disposing of the shares. We will bear all other costs, fees and expenses incurred in effecting the registration of the shares covered by this prospectus, including, without limitation, all registration and filing fees, printing fees, Nasdaq listing fees and fees and expenses of our counsel and our accountants.

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 15, 2020, we had issued and outstanding 27,424,849 shares of our common stock held by 76 stockholders of record (not including beneficial owners whose shares are held in “nominee” or “street” name).

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

Under the terms of our certificate of incorporation, our board of directors is authorized to issue up to 5,000,000 shares of “blank check” preferred stock in one or more series without stockholder approval. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock. The issuance of preferred stock could impede the completion of a merger, tender offer or other takeover attempt.

The purpose of authorizing our board of directors to issue preferred stock and determine its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions, future financings and other corporate purposes, could have the effect of making it more difficult for a third party to acquire, or could discourage a third party from seeking to acquire, a majority of our outstanding voting stock. As of the date of this prospectus, there are no shares of preferred stock outstanding, and we have no present plans to issue any shares of preferred stock.

Options and Unvested Restricted Stock

As of June 15, 2020, options to purchase an aggregate of 2,859,882 shares of our common stock, at a weighted average exercise price of \$11.70 per share, were outstanding, and 488,362 shares of unvested restricted common stock were outstanding.

Delaware Anti-Takeover Law and Certain Charter and Bylaw Provisions

Delaware Law

We are subject to Section 203 of the 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 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

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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

Resale Registration Rights

In connection with the private placement that we completed in June 2020, we entered into a registration rights agreement with the selling stockholders under which we have agreed to file the registration statement of which this prospectus is a part with the SEC, covering the resale of the 4,029,411 shares of common stock issued in such June 2020 private placement.

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.

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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.

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."

SELLING STOCKHOLDERS

On June 9, 2020, we entered into a securities purchase agreement, or the Purchase Agreement, with the selling stockholders, pursuant to which we issued and sold 4,029,411 shares of our common stock at a price of \$17.00 per share for gross proceeds of approximately \$68.5 million, which we refer to as the Private Placement. The Private Placement closed on June 9, 2020.

In connection with the Private Placement, we entered into a registration rights agreement with the selling stockholders, dated as of June 9, 2020, or the Registration Rights Agreement, pursuant to which we agreed to file a registration statement with the SEC covering the resale of the shares of common stock sold in the Private Placement. We agreed to file such registration statement within 15 days after the date of the Registration Rights Agreement. The Registration Rights Agreement includes customary indemnification rights in connection with the registration statement. The registration statement of which this prospectus is a part has been filed in accordance with the Registration Rights Agreement.

The foregoing summary descriptions of the Purchase Agreement and the Registration Rights Agreement do not purport to be complete and are qualified in their entirety by reference to the full text of such documents, which were filed as exhibits to our Current Report on Form 8-K, dated June 10, 2020, and are incorporated by reference herein.

The table below sets forth, to our knowledge, information concerning the beneficial ownership of shares of our common stock held by the selling stockholders as of June 15, 2020. The information in the table below with respect to the selling stockholders has been obtained from the selling stockholders. The selling stockholders may sell all, some or none of the shares of common stock subject to this prospectus. See “Plan of Distribution.”

The number of shares of common stock beneficially owned prior to the offering for each selling stockholder includes all shares of common stock held by such selling stockholder as of June 15, 2020, including the shares of common stock purchased by such selling stockholder in the June 2020 private placement. The percentages of shares of common stock beneficially owned prior to and after the offering are based on 27,424,849 shares of common stock outstanding as of June 15, 2020, which includes the shares of common stock offered by this prospectus.

Beneficial ownership is determined in accordance with the rules of the SEC and includes voting or investment power with respect to shares. Unless otherwise indicated below, to our knowledge, all selling stockholders named in the table have sole voting and investment power with respect to their shares of common stock. The inclusion of any shares in this table does not constitute an admission of beneficial ownership for the selling stockholders named below.

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None of the selling stockholders has held any position or office, or has otherwise had a material relationship, with us or our subsidiary within the past three years, other than as described below.

<u>Name of Selling Stockholder</u>	<u>Shares of Common Stock Beneficially Owned Prior to Offering</u>		<u>Number of Shares of Common Stock Being Offered</u>	<u>Shares of Common Stock to be Beneficially Owned After Offering (1)</u>	
	<u>Number</u>	<u>Percentage</u>		<u>Number</u>	<u>Percentage</u>
Entities associated with EcoR1 Capital, LLC (2)	882,353	3.2%	882,353	—	—
Alyeska Funds (3)	882,353	3.2%	882,353	—	—
Boxer Capital, LLC (4)	705,882	2.6%	705,882	—	—
Casdin Partners Master Fund, L.P. (5)	1,680,461	6.1%	441,176	1,239,285	4.5%
Perceptive Life Sciences Master Fund LTD (6)	294,118	1.1%	294,118	—	—
Samsara BioCapital, L.P. (7)	294,118	1.1%	294,118	—	—
Entities affiliated with Monashee Investment Management LLC (8)	294,118	1.1%	294,118	—	—
Foresite Capital Fund IV, L.P. (9)	1,133,948	4.1%	235,293	898,655	3.3%

- (1) We do not know when or in what amounts a selling stockholder may offer shares for sale. The selling stockholders might not sell any or all of the shares offered by this prospectus. Because the selling stockholders may offer all or some of the shares pursuant to this offering, and because there are currently no agreements, arrangements or understandings with respect to the sale of any of the shares, we cannot estimate the number of the shares that will be held by the selling stockholders after completion of the offering. However, for purposes of this table, we have assumed that, after completion of the offering, none of the shares covered by this prospectus will be held by the selling stockholders.
- (2) Consists of (i) 747,472 shares of common stock held by EcoR1 Capital Fund Qualified, L.P. and (ii) 134,881 shares of common stock held by EcoR1 Capital Fund, L.P., or the EcoR1 Funds. Oleg Nodelman is the Managing Director and owns and controls EcoR1 Capital, LLC the general partner of the EcoR1 Funds, and has voting and disposition power over the shares held by the EcoR1 Funds. As a result, Mr. Nodelman may be deemed to have beneficial ownership of the securities that are held by the EcoR1 Funds. The address of the EcoR1 Funds is 357 Tehama Street #3, San Francisco, CA 94103.
- (3) Consists of (i) 874,136 shares of common stock held by Alyeska Master Fund, L.P. and (ii) 8,217 shares of common stock held by Alyeska Master Fund 3, L.P., or collectively, the Alyeska Funds. Alyeska Investment Group, L.P., the investment manager of the Alyeska Funds has voting and investment control of the shares held directly by the Alyeska Funds. Anand Parekh, Chief Executive Officer of Alyeska Investment Group, L.P., has the power to vote and dispose of these shares and may be deemed to be the beneficial owner of these shares. Mr. Parekh disclaims beneficial ownership over the shares held by the Alyeska Funds. The business address of the Alyeska Funds is 77 West Wacker, Suite 700, Chicago, Illinois 60601.
- (4) Consists of shares of common stock held by Boxer Capital LLC, or Boxer. Boxer Asset Management Inc. is the managing member and majority owner of Boxer. Joseph C. Lewis is the sole indirect beneficial owner of Boxer Asset Management Inc. Boxer Asset Management Inc. and Joseph C. Lewis may be deemed to have shared voting and investment power over the shares held by Boxer. Boxer Asset Management Inc. and Joseph C. Lewis disclaim beneficial ownership of such shares, except to the extent of their pecuniary interest therein. The address of Boxer is 11682 El Camino Real, Suite 320, San Diego, CA 92130.
- (5) Consists of shares of common stock held by Casdin Partners Master Fund, L.P. Such securities may be deemed to be indirectly beneficially owned by (i) Casdin Capital, LLC, the investment adviser to Casdin Partners Master Fund, L.P., (ii) Casdin Partners GP, LLC, the general partner of Casdin Partners Master Fund L.P., and (iii) Eli Casdin, the managing member of Casdin Capital, LLC and Casdin Partners GP, LLC. Each of Casdin Capital, LLC, Casdin Partners GP, LLC and Eli Casdin disclaims beneficial ownership of such securities except to the extent of their respective pecuniary interest therein. The address of Casdin Capital is 1350 Avenue of the Americas, Suite 2600, New York, NY 10019.

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- (6) Consists of shares held by Perceptive Life Sciences Master Fund LTD, or the Master Fund. Perceptive Advisors LLC is the investment manager to the Master Fund and may be deemed to beneficially own the securities directly held by the Master Fund. Joseph Edelman is the managing member of Perceptive Advisors LLC. Perceptive Advisors LLC and Mr. Edelman may be deemed to beneficially own the shares held by the Master Fund. The address of Perceptive is 51 Astor Place, 10th Floor, New York, NY 10003.
- (7) Consists of shares of common stock held by Samsara BioCapital, L.P., or Samsara. Samsara Biocapital GP, LLC, or Samsara GP, is the general partner of Samsara. The investment manager of Samsara is Samsara BioCapital, LLC. Dr. Srinivas Akkaraju, M.D., Ph.D. is the managing member of Samsara BioCapital LLC, and Dr. Akkaraju may be deemed to have shared voting and investment power of the shares held by Samsara. Dr. Akkaraju disclaims beneficial ownership of the shares beneficially owned by Samsara, except to the extent of his pecuniary interest therein. The address of Samsara is 628 Middlefield Road, Palo Alto, California 94301.
- (8) Consists of (i) 133,690 shares of common stock held by BEMAP Master Fund LTD, (ii) 80,214 shares of common stock held by Monashee Solitario Fund LP, (iii) 60,160 shares of common stock held by Monashee Pure Alpha SPV I LP and (iv) 20,054 shares of common stock held by SFL SPV I LLC, referred to collectively as the Monashee Funds. Monashee Investment Management LLC is the Investment Advisor for each of the Monashee Funds. The Partners/officers of Monashee Investment Management LLC are Tom Wynn, Gerald Coughlan and Jeff Muller. These individuals may be deemed to have shared voting and investment power of the shares held by the Monashee Funds. Each of Tom Wynn, Gerald Coughlan and Jeff Muller disclaims beneficial ownership over these shares, except to the extent of his or her pecuniary interest therein. The address for Monashee Investment Management LLC is 125 High Street, 28th Floor, Boston, MA 02110.
- (9) Consists of shares of common stock held by Foresite Capital Fund, IV, L.P., or FCF IV. Foresite Capital Management IV, LLC, or FCM IV, the general partner of FCF IV, may be deemed to have sole voting and dispositive power over these shares. James B. Tananbaum, in his capacity as managing member of FCM IV, may be deemed to have sole voting and dispositive power over these shares. Each of FCM IV and its members and Mr. Tananbaum disclaims beneficial ownership of any of these shares except to the extent of any pecuniary interest therein. The address of FCF IV is 600 Montgomery Street, Suite 4500, San Francisco, CA 94111. Mr. Tananbaum served on our board of directors until his resignation, which was effective on April 3, 2019.

PLAN OF DISTRIBUTION

The selling stockholders, which as used herein includes donees, pledgees, transferees or other successors-in-interest selling shares of common stock or interests in shares of common stock received after the date of this prospectus from a selling stockholder as a gift, pledge, partnership distribution or other transfer, may, from time to time, sell, transfer or otherwise dispose of any or all of their shares of common stock or interests in shares of common stock on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These dispositions may be at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market price, at varying prices determined at the time of sale, or at negotiated prices.

The selling stockholders may use any one or more of the following methods when disposing of shares or interests therein:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent, but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- short sales effected after the date the registration statement of which this prospectus is a part is declared effective by the SEC;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- broker-dealers may agree with the selling stockholders to sell a specified number of such shares at a stipulated price per share;
- a combination of any such methods of sale; and
- any other method permitted by applicable law.

The selling stockholders may, from time to time, pledge or grant a security interest in some or all of the shares of common stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of common stock, from time to time, under this prospectus, or under an amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act, amending the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus. The selling stockholders also may transfer the shares of common stock in other circumstances, in which case the transferees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

In connection with the sale of our common stock or interests therein, the selling stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the common stock in the course of hedging the positions they assume. The selling stockholders may also sell shares of our common stock short and deliver these securities to close out their short positions, or loan or pledge the common stock to broker-dealers that in turn may sell these securities. The selling stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

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The aggregate proceeds to the selling stockholders from the sale of the common stock offered by them will be the purchase price of the common stock less discounts or commissions, if any. Each of the selling stockholders reserves the right to accept and, together with their agents from time to time, to reject, in whole or in part, any proposed purchase of common stock to be made directly or through agents. We will not receive any of the proceeds from this offering.

The selling stockholders also may resell all or a portion of the shares in open market transactions in reliance upon Rule 144 under the Securities Act, provided that they meet the criteria and conform to the requirements of that rule.

The selling stockholders and any underwriters, broker-dealers or agents that participate in the sale of the common stock or interests therein may be “underwriters” within the meaning of Section 2(11) of the Securities Act. Any discounts, commissions, concessions or profit they earn on any resale of the shares may be underwriting discounts and commissions under the Securities Act. Selling stockholders who are “underwriters” within the meaning of Section 2(11) of the Securities Act will be subject to the prospectus delivery requirements of the Securities Act.

To the extent required, the shares of our common stock to be sold, the names of the selling stockholders, the respective purchase prices and public offering prices, the names of any agent, dealer or underwriter, and any applicable commissions or discounts with respect to a particular offer will be set forth in an accompanying prospectus supplement or, if appropriate, a post-effective amendment to the registration statement that includes this prospectus.

In order to comply with the securities laws of some states, if applicable, the common stock may be sold in these jurisdictions only through registered or licensed brokers or dealers. In addition, in some states the common stock may not be sold unless it has been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

We have advised the selling stockholders that the anti-manipulation rules of Regulation M under the Exchange Act may apply to sales of shares in the market and to the activities of the selling stockholders and their affiliates. In addition, to the extent applicable, we will make copies of this prospectus (as it may be supplemented or amended from time to time) available to the selling stockholders for the purpose of satisfying the prospectus delivery requirements of the Securities Act. The selling stockholders may indemnify any broker-dealer that participates in transactions involving the sale of the shares against certain liabilities, including liabilities arising under the Securities Act.

We have agreed to indemnify the selling stockholders against liabilities, including liabilities under the Securities Act and state securities laws, relating to the registration of the shares offered by this prospectus.

We have agreed with the selling stockholders to use commercially reasonable efforts to cause the registration statement of which this prospectus constitutes a part effective and to remain continuously effective until the earlier of (1) such time as all of the shares covered by this prospectus have been disposed of pursuant to and in accordance with such registration statement or (2) the date on which all of the shares may be sold without restriction pursuant to Rule 144 of the Securities Act.

LEGAL MATTERS

The validity of the shares of our common stock offered hereby is being passed upon for us 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.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other documents 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 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 our securities. 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.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to incorporate by reference much of the information we file with it, 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. Any statement contained in a previously filed document incorporated by reference will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus modifies or replaces that statement. 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 Exchange Act after the date of this prospectus and prior to the sale of all the shares covered by this prospectus, other than the portions of those documents not deemed to be filed.

- Our Annual Report on Form 10-K for the year ended December 31, 2019, filed with the SEC on [March 5, 2020](#);
- Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2020, filed with the SEC on [May 13, 2020](#);
- Our Current Reports on Form 8-K, filed with the SEC on [January 6, 2020](#), [April 2, 2020](#), [June 10, 2020](#) and [June 11, 2020](#);
- Our Definitive Proxy Statement on Schedule 14A for the 2020 Annual Meeting of Stockholders filed with the SEC on [April 29, 2020](#);
- 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; and
- Any other filings we make pursuant to the Exchange Act after the date of filing the initial registration statement and prior to effectiveness of the registration statement.

We will furnish without charge to you, on written or oral request, a copy of any or all of the documents incorporated by reference in this prospectus, including exhibits to these documents. You should direct any requests for documents to Fulcrum Therapeutics, Inc., 26 Landsdowne Street, Cambridge, Massachusetts 02139 or by telephone at (617) 651-8851. These documents may also be found on our website at the address stated above.

4,029,411 Shares



Common Stock

Prospectus

, 2020

PART II
INFORMATION NOT REQUIRED IN PROSPECTUS

Item 13. Other Expenses of Issuance and Distribution.

The following table sets forth the various expenses to be incurred in connection with the sale and distribution of the securities being registered hereby, all of which will be borne by us (except any underwriting discounts and commissions and expenses incurred by the selling stockholders for brokerage, accounting, tax or legal services or any other expenses incurred by the selling stockholders in disposing of the shares). All amounts shown are estimates except the Securities and Exchange Commission, or SEC, registration fee.

	Amount
SEC registration fee	\$ 8,771
Accounting fees and expenses	10,000
Legal fees and expenses	50,000
Miscellaneous fees and expenses	5,000
Total expenses	<u>\$73,771</u>

Item 14. Indemnification of Directors and Officers.

Section 102 of the Delaware General Corporation Law, or the DGCL, permits a corporation to eliminate the personal liability of its directors or its stockholders for monetary damages for a breach of fiduciary duty as a director, except where the director breached his or her duty of loyalty, failed to act in good faith, engaged in intentional misconduct or knowingly violated a law, authorized the payment of a dividend or approved a stock repurchase in violation of Delaware corporate law or obtained an improper personal benefit. Our certificate of incorporation provides that no director shall be personally liable to us or our stockholders for monetary damages for any breach of fiduciary duty as a director, notwithstanding any provision of law imposing such liability, except to the extent that the DGCL prohibits the elimination or limitation of liability of directors for breaches of fiduciary duty.

Section 145 of the DGCL provides that a corporation has the power to indemnify a director, officer, employee or agent of the corporation and certain other persons serving at the request of the corporation in related capacities against expenses (including attorneys' fees), judgments, fines and amounts paid in settlements actually and reasonably incurred by the person in connection with an action, suit or proceeding to which he or she is or is threatened to be made a party by reason of such position, if such person acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the corporation, and, in any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful, except that, in the case of actions brought by or in the right of the corporation, no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or other adjudicating court determines that, despite the adjudication of liability but in view of all of the circumstances of the case, such person is fairly and reasonably entitled to indemnification for such expenses which the Court of Chancery or such other court shall deem proper.

Our certificate of incorporation provides that we will indemnify each person who was or is a party or threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of us), by reason of the fact that he or she is or was, or has agreed to become, our director or officer, or is or was serving, or has agreed to serve, at our request as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (all such persons being referred to herein as an Indemnitee), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding and any appeal therefrom if such Indemnitee acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, our best interests, and, with respect to any criminal action or proceeding, he or she had no reasonable cause to believe his or her conduct was unlawful.

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Our certificate of incorporation also provides that we will indemnify any Indemnitee who was or is a party to an action or suit by or in the right of us to procure a judgment in our favor by reason of the fact that the Indemnitee is or was, or has agreed to become, our director or officer, or is or was serving, or has agreed to serve, at our request as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise, or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees) and, to the extent permitted by law, amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding, and any appeal therefrom, if the Indemnitee acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, our best interests, except that no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to us, unless a court determines that, despite such adjudication but in view of all of the circumstances, he or she is entitled to indemnification of such expenses. Notwithstanding the foregoing, to the extent that any Indemnitee has been successful, on the merits or otherwise, he or she will be indemnified by us against all expenses (including attorneys' fees) actually and reasonably incurred by him or her or on his or her behalf in connection therewith. If we do not assume the defense, expenses must be advanced to an Indemnitee under certain circumstances.

In addition, we have entered into indemnification agreements with all of our executive officers and directors. In general, these agreements provide that we will indemnify the executive officer or director to the fullest extent permitted by law for claims arising in his or her capacity as an executive officer or director of our company or in connection with his or her service at our request for another corporation or entity. The indemnification agreements also provide for procedures that will apply in the event that an executive officer or director makes a claim for indemnification and establish certain presumptions that are favorable to the executive officer or director.

We maintain a general liability insurance policy that covers certain liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers.

The registration rights agreement we entered into in connection with the private placement of our common stock in June 2020 provides that the selling stockholders will indemnify, under certain conditions, our directors and officers (as well as certain other persons) against certain liabilities arising in connection with this registration statement.

Insofar as the foregoing provisions permit indemnification of directors, executive officers or persons controlling us for liability arising under the Securities Act of 1933, as amended, or the Securities Act, we have been informed that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

Item 15. Recent Sales of Unregistered Securities.

Set forth below is information regarding shares of our preferred stock, shares of our common stock and stock options granted by us within the past three years that were not registered under the Securities Act. Also included is the consideration, if any, received by us for such shares and options and information relating to the section of the Securities Act, or rule of the SEC, under which exemption from registration was claimed.

(a) Issuances of Preferred Stock

In connection with preparing for our initial public offering, we effected a one-for-seven reverse stock split of our common stock. The reverse stock split became effective on July 5, 2019. The par value and authorized shares of preferred stock were not adjusted as a result of the reverse stock split. The preferred stock share and price per preferred stock share amounts in this paragraph (a) of Item 15 have not been retroactively adjusted to give effect to this reverse stock split.

On January 4, 2018, we issued and sold 6,333,334 shares of our Series A preferred stock to two investors at a price per share of \$1.00 in cash, for an aggregate purchase price of \$6,333,334.

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On March 13, 2018, we issued and sold 6,333,333 shares of our Series A preferred stock to two investors at a price per share of \$1.00 in cash, for an aggregate purchase price of \$6,333,333.

On May 9, 2018, we issued and sold 6,333,333 shares of our Series A preferred stock to two investors at a price per share of \$1.00 in cash, for an aggregate purchase price of \$6,333,333.

On June 6, 2018, we issued and sold 6,333,334 shares of our Series A preferred stock to two investors at a price per share of \$1.00 in cash, for an aggregate purchase price of \$6,333,334.

On August 24, 2018, we issued and sold 40,000,000 shares of our Series B preferred stock to 20 investors at a price per share of \$2.00 in cash, for an aggregate purchase price of \$80,000,000.

On February 8, 2019, we issued 12,500,000 shares of our Series B preferred stock to one investor in exchange for a license.

No underwriters were involved in the foregoing issuances of securities. The securities described in this section (a) of Item 15 were issued to investors in reliance upon the exemption from the registration requirements of the Securities Act, as set forth in Section 4(a)(2) under the Securities Act and, in certain cases, Regulation D thereunder, relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required. All purchasers received written disclosures that the securities had not been registered under the Securities Act and that any resale must be made pursuant to a registration statement or an available exemption from such registration.

(b) Issuances of Common Stock

Between June 22, 2017 and July 12, 2019, we issued an aggregate of 486,661 shares of restricted common stock, for cash with purchase prices of \$0.07 per share, to employees, directors, advisors or consultants pursuant to our 2016 Stock Incentive Plan.

The shares of common stock described above were issued pursuant to written compensatory plans or arrangements with our employees, directors, advisors and consultants, in reliance on the exemption provided by Rule 701 promulgated under the Securities Act, or pursuant to Section 4(a)(2) under the Securities Act, relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required. All recipients either received adequate information about our company or had access, through employment or other relationships, to such information.

On June 9, 2020, we entered into a securities purchase agreement with certain institutional accredited investors, or the Purchasers, pursuant to which we, in a private placement, agreed to issue and sell to the Purchasers 4,029,411 shares of our common stock at a price of \$17.00 per share for total gross proceeds to us of approximately \$68.5 million.

No underwriters were involved in the issuance of these shares of common stock to the Purchasers. The shares of common stock were issued to the Purchasers in reliance upon the exemption from the registration requirements of the Securities Act, as set forth in Section 4(a)(2) under the Securities Act and/or Regulation D promulgated thereunder relative to transactions by an issuer not involving any public offering. Each of the Purchasers represented that they were accredited investors and were acquiring the shares of common stock for their own account for investment purposes only and not with a view to, or for sale in connection with, any distribution thereof and that they could bear the risks of the investment and could hold the securities for an indefinite period of time and appropriate legends were affixed to the instruments representing such securities issued in such transactions.

(c) Stock Option Grants and Option Exercises

Between June 22, 2017 and July 12, 2019, we granted options to purchase an aggregate of 1,622,382 shares of common stock, with exercise prices ranging from \$4.83 to \$11.06 per share, to our employees, directors, advisors

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or consultants pursuant to our 2016 Stock Incentive Plan. Between June 22, 2017 and the filing of our registration statement on Form S-8 on August 26, 2019, we issued 33,561 shares of our common stock upon the exercise of stock options outstanding under our 2016 Stock Incentive Plan for aggregate consideration of \$0.3 million.

The stock options and the shares of common stock issued upon the exercise of stock options described in this section (c) of Item 15 were issued pursuant to written compensatory plans or arrangements with our employees, directors, advisors and consultants, in reliance on the exemption provided by Rule 701 promulgated under the Securities Act, or pursuant to Section 4(a)(2) under the Securities Act, relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required. All recipients either received adequate information about our company or had access, through employment or other relationships, to such information.

Item 16. Exhibits and Financial Statement Schedules.

(a) Exhibits

Exhibit Number	Description
3.1	<u>Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-38978) filed with the Securities and Exchange Commission on July 22, 2019).</u>
3.2	<u>Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K (File No. 001-38978) filed with the Securities and Exchange Commission on July 22, 2019).</u>
4.1	<u>Specimen Stock Certificate evidencing shares of common stock (incorporated by reference to Exhibit 4.1 to the Registrant's Registration Statement on Form S-1 (File No. 333-232260) filed with the Securities and Exchange Commission on June 21, 2019).</u>
5.1	<u>Opinion of Wilmer Cutler Pickering Hale and Dorr LLP.</u>
10.1	<u>Amended and Restated Investors' Rights Agreement, dated as of August 24, 2018, by and among the Registrant and the other parties thereto (incorporated by reference to Exhibit 10.1 to the Registrant's Registration Statement on Form S-1 (File No. 333-232260) filed with the Securities and Exchange Commission on June 21, 2019).</u>
10.2*	<u>2016 Stock Incentive Plan, as amended (incorporated by reference to Exhibit 10.2 to the Registrant's Registration Statement on Form S-1 (File No. 333-232260) filed with the Securities and Exchange Commission on June 21, 2019).</u>
10.3*	<u>Form of Incentive Stock Option Agreement under the 2016 Stock Incentive Plan (incorporated by reference to Exhibit 10.3 to the Registrant's Registration Statement on Form S-1 (File No. 333-232260) filed with the Securities and Exchange Commission on June 21, 2019).</u>
10.4*	<u>Form of Non-Statutory Stock Option Agreement under the 2016 Stock Incentive Plan (incorporated by reference to Exhibit 10.4 to the Registrant's Registration Statement on Form S-1 (File No. 333-232260) filed with the Securities and Exchange Commission on June 21, 2019).</u>
10.5*	<u>Form of Restricted Stock Agreement under the 2016 Stock Incentive Plan (incorporated by reference to Exhibit 10.5 to the Registrant's Registration Statement on Form S-1 (File No. 333-232260) filed with the Securities and Exchange Commission on June 21, 2019).</u>
10.6*	<u>2019 Stock Incentive Plan (incorporated by reference to Exhibit 10.6 to Amendment No. 1 to Registrant's Registration Statement on Form S-1 (File No. 333-232260) filed with the Securities and Exchange Commission on July 8, 2019).</u>
10.7*	<u>Form of Stock Option Agreement under the 2019 Stock Incentive Plan (incorporated by reference to Exhibit 10.7 to Amendment No. 1 to Registrant's Registration Statement on Form S-1 (File No. 333-232260) filed with the Securities and Exchange Commission on July 8, 2019).</u>

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Exhibit Number	Description
10.8*	<u>2019 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.8 to Amendment No. 1 to Registrant's Registration Statement on Form S-1 (File No. 333-232260) filed with the Securities and Exchange Commission on July 8, 2019).</u>
10.9*	<u>Summary of Non-Employee Director Compensation Program (incorporated by reference to Exhibit 10.9 to Amendment No. 1 to Registrant's Registration Statement on Form S-1 (File No. 333-232260) filed with the Securities and Exchange Commission on July 8, 2019).</u>
10.10†	<u>Right of Reference and License Agreement, dated as of February 8, 2019, by and among the Registrant, GlaxoSmithKline Intellectual Property (No. 2) Limited, GlaxoSmithKline LLC and Glaxo Group Limited (incorporated by reference to Exhibit 10.10 to the Registrant's Registration Statement on Form S-1 (File No. 333-232260) filed with the Securities and Exchange Commission on June 21, 2019).</u>
10.11	<u>Lease for 26 Landsdowne Street, dated November 22, 2017, by and between the UP 26 Landsdowne, LLC and the Registrant (incorporated by reference to Exhibit 10.11 to the Registrant's Registration Statement on Form S-1 (File No. 333-232260) filed with the Securities and Exchange Commission on June 21, 2019).</u>
10.12*	<u>Form of Employment Agreement for Executive Officers (incorporated by reference to Exhibit 10.12 to Amendment No. 1 to Registrant's Registration Statement on Form S-1 (File No. 333-232260) filed with the Securities and Exchange Commission on July 8, 2019).</u>
10.13*	<u>Employment Agreement, dated June 30, 2019, by and between the Registrant and Robert J. Gould (incorporated by reference to Exhibit 10.13 to Amendment No. 2 to Registrant's Registration Statement on Form S-1 (File No. 333-232260) filed with the Securities and Exchange Commission on July 12, 2019).</u>
10.14*	<u>Employment Agreement, dated July 3, 2019, by and between the Registrant and Bryan Stuart (incorporated by reference to Exhibit 10.14 to Amendment No. 2 to Registrant's Registration Statement on Form S-1 (File No. 333-232260) filed with the Securities and Exchange Commission on July 12, 2019).</u>
10.15*	<u>Employment Agreement, dated July 18, 2019, by and between the Registrant and Owen Wallace (incorporated by reference to Exhibit 10.1 to Registrant's Quarterly Report on Form 10-Q (File No. 001-38978) filed with the Securities and Exchange Commission on May 13, 2020).</u>
10.16*	<u>Form of Indemnification Agreement between the Registrant and each of its Executive Officers and Directors (incorporated by reference to Exhibit 10.15 to Registrant's Registration Statement on Form S-1 (File No. 333-232260) filed with the Securities and Exchange Commission on June 21, 2019).</u>
10.17†	<u>Collaboration and License Agreement, dated as of December 20, 2019, by and between the Registrant and Acceleron Pharma Inc. (incorporated by reference to Exhibit 10.17 to Registrant's Annual Report on Form 10-K (File No. 001-38978) filed with the Securities and Exchange Commission on March 5, 2020).</u>
10.18	<u>Securities Purchase Agreement, dated June 9, 2020, by and among the Registrant and the other parties thereto (incorporated by reference to Exhibit 10.1 to Registrant's Current Report on Form 8-K (File No. 001-38978) filed with the Securities and Exchange Commission on June 10, 2020).</u>
10.19	<u>Registration Rights Agreement, dated June 9, 2020, by and among the Registrant and the other parties thereto (incorporated by reference to Exhibit 10.2 to Registrant's Current Report on Form 8-K (File No. 001-38978) filed with the Securities and Exchange Commission on June 10, 2020).</u>
21.1	<u>Subsidiary of the Registrant (incorporated by reference to Exhibit 21.1 to Registrant's Annual Report on Form 10-K (File No. 001-38978) filed with the Securities and Exchange Commission on March 5, 2020).</u>
23.1	<u>Consent of Ernst & Young LLP, independent registered public accounting firm.</u>
23.2	<u>Consent of Wilmer Cutler Pickering Hale and Dorr LLP (included in Exhibit 5.1).</u>
24.1	<u>Power of Attorney (included on signature page).</u>

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* Indicates management contract or compensatory plan

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

(b) Financial Statement Schedules

No financial statement schedules are provided because the information called for is not required or is shown either in the financial statements or the related notes.

Item 17. Undertakings.

(a) The undersigned Registrant hereby undertakes:

- (1) To file, during any period in which offers or sales are being made, a post-effective amendment to this Registration Statement:
 - (i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933, as amended (the "Securities Act");
 - (ii) To reflect in the prospectus any facts or events arising after the effective date of this Registration Statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in this Registration Statement. Notwithstanding the foregoing, any increase or decrease in the volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Securities and Exchange Commission (the "Commission") pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective Registration Statement; and
 - (iii) To include any material information with respect to the plan of distribution not previously disclosed in this Registration Statement or any material change to such information in this Registration Statement;

provided, however, that paragraphs (1)(i), (1)(ii) and (1)(iii) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in periodic reports filed with or furnished to the Commission by the Registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), that are incorporated by reference in this Registration Statement.

- (2) That, for the purposes of determining any liability under the Securities Act, each post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at the time shall be deemed to be the initial *bona fide* offering thereof.
- (3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.
- (4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser, each prospectus filed pursuant to Rule 424(b) as part of a registration statement relating to an offering, other than registration statements relying on Rule 430B or other than prospectuses filed in reliance on Rule 430A, shall be deemed to be part of and included in the registration statement as of the date it is first used after effectiveness; provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such first use, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such date of first use.

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- (b) The Registrant hereby undertakes that, for purposes of determining any liability under the Securities Act, each filing of the Registrant's annual report pursuant to Section 13(a) or 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Exchange Act) that is incorporated by reference in this Registration Statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.
- (c) Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Registrant pursuant to the indemnification provisions described herein, or otherwise, the Registrant has been advised that in the opinion of the Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Cambridge, Commonwealth of Massachusetts, on this 22nd day of June, 2020.

FULCRUM THERAPEUTICS, INC.

By: /s/ Robert J. Gould

Robert J. Gould, Ph.D.

President and Chief Executive Officer

SIGNATURES AND POWER OF ATTORNEY

We, the undersigned officers and directors of Fulcrum Therapeutics, Inc., hereby severally constitute and appoint Robert J. Gould and Bryan Stuart, and each of them singly (with full power to each of them to act alone), our true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution in each of them for him or her and in his or her name, place and stead, and in any and all capacities, to sign any and all amendments (including post-effective amendments) to this Registration Statement, and any other registration statement for the same offering pursuant to Rule 462(b) under the Securities Act of 1933, and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite or necessary to be done in and about the premises, as full to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents or any of them, or their, his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this Registration Statement has been signed by the following persons in the capacities held on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Robert J. Gould</u> Robert J. Gould, Ph.D.	President and Chief Executive Officer, Director (Principal Executive Officer)	June 22, 2020
<u>/s/ Bryan Stuart</u> Bryan Stuart	Chief Operating Officer (Principal Financial Officer)	June 22, 2020
<u>/s/ Peter Thomson</u> Peter Thomson	Vice President, Finance & Accounting (Principal Accounting Officer)	June 22, 2020
<u>/s/ Mark Levin</u> Mark Levin	Chairman of the Board	June 22, 2020
<u>/s/ James J. Collins</u> James J. Collins, Ph.D.	Director	June 22, 2020
<u>/s/ Katina Dorton</u> Katina Dorton	Director	June 22, 2020
<u>/s/ Alan Ezekowitz</u> Alan Ezekowitz, MBChB, D. Phil	Director	June 22, 2020
<u>/s/ James Geraghty</u> James Geraghty	Director	June 22, 2020
<u>/s/ Kate Haviland</u> Kate Haviland	Director	June 22, 2020

June 22, 2020

Fulcrum Therapeutics, Inc.
26 Landsdowne Street
Cambridge, MA 02139

Re: Registration Statement on Form S-1

Ladies and Gentlemen:

This opinion is furnished to you in connection with a Registration Statement on Form S-1 (the "Registration Statement") filed with the Securities and Exchange Commission (the "Commission") under the Securities Act of 1933, as amended (the "Securities Act"), for the registration of the resale of an aggregate of 4,029,411 shares (the "Shares") of common stock, \$0.001 par value per share (the "Common Stock"), of Fulcrum Therapeutics, Inc., a Delaware corporation (the "Company"). All of the Shares are being registered for resale on behalf of certain stockholders of the Company (the "Selling Stockholders").

We are acting as counsel for the Company in connection with the registration for resale of the Shares. We have examined signed copies of the Registration Statement as filed with the Commission. We have also examined and relied upon minutes of meetings of the Board of Directors of the Company as provided to us by the Company, the Restated Certificate of Incorporation and Amended and Restated Bylaws of the Company, each as restated and/or amended to date, and such other documents as we have deemed necessary for purposes of rendering the opinions hereinafter set forth.

In our examination of the foregoing documents, we have assumed the genuineness of all signatures, the authenticity of all documents submitted to us as originals, the conformity to original documents of all documents submitted to us as copies, the authenticity of the originals of such latter documents and the legal competence of all signatories to such documents.

Our opinion below, insofar as it relates to the Shares being fully paid, is based solely on a certificate of the Chief Operating Officer of the Company confirming the Company's receipt of the consideration called for by the applicable resolutions authorizing the issuance of such Shares.

We assume that the appropriate action will be taken, prior to the offer and sale of the Shares by the Selling Stockholders, to register and qualify the Shares for sale under all applicable state securities or "blue sky" laws.

Wilmer Cutler Pickering Hale and Dorr LLP, 60 State Street, Boston, Massachusetts 02109

Beijing Berlin Boston Brussels Denver Frankfurt London Los Angeles New York Palo Alto San Francisco Washington

We express no opinion herein as to the laws of any state or jurisdiction other than the General Corporation Law of the State of Delaware and the federal laws of the United States of America.

Based upon and subject to the foregoing, we are of the opinion that the Shares have been duly authorized for issuance and are validly issued, fully paid and nonassessable. It is understood that this opinion is to be used only in connection with the offer and sale of the Shares while the Registration Statement is in effect.

Please note that we are opining only as to the matters expressly set forth herein, and no opinion should be inferred as to any other matters. This opinion is based upon currently existing statutes, rules, regulations and judicial decisions, and we disclaim any obligation to advise you of any change in any of these sources of law or subsequent legal or factual developments which might affect any matters or opinions set forth herein.

We hereby consent to the filing of this opinion with the Commission as an exhibit to the Registration Statement in accordance with the requirements of Item 601(b)(5) of Regulation S-K under the Securities Act and to the use of our name therein and in the related Prospectus under the caption "Legal Matters." In giving such consent, we do not hereby admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations of the Commission.

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June 22, 2020

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Very truly yours,

WILMER CUTLER PICKERING
HALE AND DORR LLP

By: /s/ Lia Der Marderosian
Lia Der Marderosian, a Partner

Consent of Independent Registered Public Accounting Firm

We consent to the reference to our firm under the caption “Experts” in the Registration Statement (Form S-1) and related Prospectus of Fulcrum Therapeutics, Inc. for the registration of 4,029,411 shares of its common stock and to the incorporation by reference therein of our report dated March 5, 2020, with respect to the consolidated financial statements of Fulcrum Therapeutics, Inc. included in its Annual Report (Form 10-K) for the year ending December 31, 2019, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

Boston, Massachusetts
June 19, 2020