

PROSPECTUS SUPPLEMENT
(To prospectus dated April 28, 2022)



\$50,000,000

Common Stock

We have entered into an equity distribution agreement with Piper Sandler & Co., or Piper Sandler, dated May 9, 2022, relating to the sale of shares of our common stock offered by this prospectus supplement. In accordance with the terms of the equity distribution agreement, under this prospectus supplement we may offer and sell shares of our common stock, \$0.001 par value per share, having an aggregate offering price of up to \$50,000,000 from time to time through Piper Sandler, acting as our agent.

Our common stock is listed on The Nasdaq Global Market under the symbol "FULC". On May 6, 2022, the last sale price of our common stock as reported on The Nasdaq Global Market was \$8.63 per share.

Sales of our common stock, if any, under this prospectus supplement and the accompanying base prospectus may be made by any method permitted by law that is deemed to be an "at the market offering" as defined in Rule 415(a)(4) under the Securities Act of 1933, as amended, or the Securities Act, including sales made directly on or through The Nasdaq Global Market, the existing trading market for our common stock. Piper Sandler is not required to sell any specific amount, but will act as our sales agent using commercially reasonable efforts, consistent with its normal trading and sales practices. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

The compensation to Piper Sandler for sales of common stock sold pursuant to the equity distribution agreement will be 3.0% of the gross proceeds of any shares of common stock sold under the equity distribution agreement. See "Plan of Distribution" beginning on page S-10 for additional information regarding the compensation to be paid to Piper Sandler. In connection with the sale of the common stock on our behalf, Piper Sandler will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of Piper Sandler will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to Piper Sandler with respect to certain liabilities, including civil liabilities under the Securities Act.

Investing in our common stock involves significant risks. See "[Risk Factors](#)" beginning on page S-6 of this prospectus supplement, page 2 of the accompanying base prospectus and in the documents incorporated by reference in this prospectus supplement for a discussion of the factors you should carefully consider before deciding to purchase our common stock.

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

Piper Sandler

May 9, 2022

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement is part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC, utilizing a “shelf” registration process. Under this prospectus supplement, we may from time to time sell shares of our common stock having an aggregate offering price of up to \$50,000,000, at prices and on terms to be determined by market conditions at the time of the offering.

Before buying any of the common stock that we are offering, we urge you to carefully read this prospectus supplement, the accompanying base prospectus and all of the information in the documents that are incorporated by reference in this prospectus supplement and the accompanying base prospectus, as well as the additional information described under the headings “Where You Can Find More Information” and “Incorporation of Certain Documents by Reference.” These documents contain important information that you should consider when making your investment decision.

We provide information to you about this offering of our common stock in two separate documents that are bound together: (1) this prospectus supplement, which describes the specific details regarding this offering; and (2) the accompanying base prospectus, which provides general information, some of which may not apply to this offering. Generally, when we refer to this “prospectus,” we are referring to both documents combined. If information in this prospectus supplement is inconsistent with the accompanying base prospectus, you should rely on this prospectus supplement. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in any document incorporated by reference in this prospectus supplement that was filed with the SEC before the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement, provided that if any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference in this prospectus supplement—the statement in the document having the later date modifies or supersedes the earlier statement.

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

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

You should also read and consider the information in the documents to which we have referred you in the sections entitled “Where You Can Find More Information” and “Incorporation of Certain Documents by Reference” in this prospectus supplement.

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

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This prospectus supplement, the accompanying base prospectus and the documents incorporated by reference in each of this prospectus supplement and the accompanying base prospectus include “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. All statements, other than statements of historical fact, contained or incorporated by reference in this prospectus supplement and the accompanying base prospectus, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “might,” “plan,” “predict,” “project,” “target,” “potential,” “would,” “could,” “should,” “continue” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

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

You should read this prospectus supplement, the accompanying base prospectus, the documents incorporated by reference in this prospectus supplement and the documents that we have filed as exhibits to the registration statement of which this prospectus supplement 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 supplement and the accompanying base prospectus and incorporated by reference herein are made as of the date hereof, and we do not assume any obligation to update any forward-looking statements except as required by applicable law.

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

PROSPECTUS SUMMARY

This summary highlights certain information about us, this offering and selected information contained elsewhere in this prospectus supplement, the accompanying base prospectus and in the documents we incorporate by reference. This summary is not complete and does not contain all of the information that you should consider before making an investment decision. You should read this entire prospectus carefully, especially the risks of investing in our common stock discussed under “Risk Factors” beginning on page S-6 of this prospectus supplement and page 2 of the accompanying base prospectus, along with our consolidated financial statements and notes to those consolidated financial statements and the other documents incorporated by reference in this prospectus supplement.

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. Our most advanced product candidate, losmapimod, is in development to treat the root cause of facioscapulohumeral muscular dystrophy, or FSHD. Our other clinical product candidate is FTX-6058, which is being developed for the treatment of certain hemoglobinopathies, including sickle cell disease, or SCD and β -thalassemia. We expect to initiate REACH, a randomized, double-blind, placebo-controlled, multi-national Phase 3 clinical trial of losmapimod, our product candidate for FSHD, in the second quarter of 2022. We initiated a Phase 1b clinical trial of FTX-6058 in people with SCD in the fourth quarter of 2021, and we plan to present initial data, including measures of fetal hemoglobin, or HbF, protein induction and safety, from the ongoing 6 mg dose cohort at the European Hematology Association, or EHA, 2022 Hybrid Congress, taking place from June 9-12, 2022. Additionally, we submitted an investigational new drug application, or IND, in the fourth quarter of 2021 for FTX-6058 in other select hemoglobinopathies, including β -thalassemia, and expect to initiate a Phase 1b clinical trial in the second half of 2022.

We have developed a proprietary product engine, FulcrumSeek, that we employ to systematically identify and validate cellular drug targets that can potentially modulate gene expression to treat known root causes of genetically defined diseases. Our product engine integrates patient-derived tissue and disease-relevant cell models that we interrogate using our pharmacologically diverse and highly annotated small-molecule compound library and customized CRISPR and RNAi libraries. These screens generate tens of millions of data points and high-content imaging. We then apply computational biology and analytics to identify targets with specificity and selectivity accompanied by a comprehensive data set that significantly accelerates development. This approach led to the identification of both losmapimod for FSHD and FTX-6058 for hemoglobinopathies, as well as a robust discovery pipeline. We expect to nominate our next development candidate this year to support our fourth IND by the end of the first quarter of 2023.

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 supplement. We have included our website address in this prospectus supplement solely as an inactive textual reference.

We own or have rights, or have applied for, to trademarks, service marks and trade names that we use in connection with the operation of our business, including our corporate name, logos and website names. Other trademarks, service marks and trade names appearing in this prospectus supplement and the

accompanying base prospectus are the property of their respective owners. Solely for convenience, some of the trademarks, service marks and trade names referred to in this prospectus supplement and the accompanying base prospectus are listed without the ® and ™ symbols, but we will assert, to the fullest extent under applicable law, our rights to our trademarks, service marks and trade names.

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

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

We are also a “smaller reporting company,” meaning that the market value of our stock held by non-affiliates is less than \$700 million as of our most recently completed second fiscal quarter and our annual revenue was less than \$100 million during our most recently completed fiscal year. We may continue to be a smaller reporting company if either (i) the market value of our stock held by non-affiliates is less than \$250 million as of our most recently completed second fiscal quarter 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 Us	Shares of our common stock having an aggregate offering price of up to \$50,000,000.
Common Stock to be Outstanding Immediately After This Offering	Up to 46,477,767 shares, assuming sales of 5,793,742 shares of our common stock in this offering at a price of \$8.63 per share, which was the last reported sale price of our common stock on The Nasdaq Global Market on May 6, 2022. The actual number of shares issued will vary depending on the sales price under this offering.
Manner of Offering	“At the market” offering that may be made from time to time through our sales agent, Piper Sandler. See “Plan of Distribution” in this prospectus supplement for more information.
Use of Proceeds	We intend to use the net proceeds from the sale of securities offered under this prospectus supplement primarily for general corporate purposes, which may include working capital and capital expenditures, research and development expenses, including to fund clinical trials, regulatory submissions, commercialization, discovery and additional preclinical research and development of additional product candidates and platform enhancement, general and administrative expenses, and potential acquisitions of, or investments in, companies, technologies, products or assets that complement our business. See “Use of Proceeds” in this prospectus supplement for more information.
Risk Factors	You should read the “Risk Factors” in this prospectus supplement, the accompanying base prospectus and the other documents incorporated by reference into this prospectus supplement for a discussion of factors to consider carefully before deciding to purchase shares of our common stock.
Nasdaq Global Market Symbol	FULC

The number of shares of our common stock that will be outstanding immediately after this offering as shown above is based on 40,684,025 shares outstanding as of March 31, 2022, including 420 shares of unvested restricted stock awards subject to repurchase by us. The number of shares outstanding as of March 31, 2022 as used throughout this prospectus supplement, unless otherwise indicated, excludes:

- 6,526,973 shares of common stock issuable upon exercise of stock options outstanding as of March 31, 2022 at a weighted average exercise price of \$13.85 per share;
- 44,427 shares of common stock issuable upon vesting of restricted stock units outstanding as of March 31, 2022; and
- 953,886, 1,718,480, and 1,113,021 shares of our common stock available for future issuance as of March 31, 2022 under our 2019 Stock Incentive Plan, our 2022 Inducement Stock Incentive Plan and our 2019 Employee Stock Purchase Plan, respectively, as well as any automatic increases in the number of shares of common stock reserved under these plans.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below together with all of the other information contained in this prospectus supplement and the accompanying base prospectus and the risk factors in our most recent Annual Report on Form 10-K, our most recent Quarterly Report on Form 10-Q and in our other filings with the SEC that we make from time to time, which are incorporated by reference in this prospectus supplement, together with other information in this prospectus supplement, the accompanying base prospectus and the information and documents incorporated by reference in this prospectus supplement and the accompanying base prospectus, and in any prospectus supplement or free writing prospectus that we authorize for use in connection with this offering. If any of the following risks actually occur, our business, prospects, operating results and financial condition could suffer materially. In such event, the trading price of our common stock could decline and you might lose all or part of your investment.

Risks Related to This Offering

Sale of a substantial number of shares of our common stock, including by us, could cause the market price of our common stock to drop significantly, even if our business is doing well.

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

Moreover, holders of a substantial number of shares of our common stock have rights, subject to specified conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders.

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

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

Our management may invest or spend the proceeds of this offering in ways with which you may not agree or in ways that may not yield a return.

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

In addition, the issuance from time to time of shares of our common stock in this offering, or our ability to issue these shares of common stock in this offering, could result in resales of our common stock by our current stockholders concerned about the potential dilution of their holdings. In turn, these resales could have the effect of depressing the market price for our common stock.

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Purchasers will experience immediate dilution in the book value per share of the common stock purchased in the offering.

The shares sold in this offering, if any, will be sold from time to time at various prices. However, we expect that the offering price of our common stock will be substantially higher than the net tangible book value per share of our outstanding common stock. After giving effect to the sale of shares of our common stock in the aggregate amount of \$50,000,000 at an assumed offering price of \$8.63 per share, the last sale price of our common stock on May 6, 2022 on The Nasdaq Global Market, and after deducting estimated commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of March 31, 2022 would have been approximately \$237.5 million, or approximately \$5.11 per share. This represents an immediate increase in as adjusted net tangible book value of approximately \$0.46 per share to our existing stockholders and an immediate dilution in as adjusted net tangible book value of approximately \$3.52 per share to purchasers of our common stock in this offering. See “Dilution” in this prospectus supplement for more information.

You may experience future dilution as a result of future equity offerings.

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock at prices that may not be the same as the price per share in this offering. We may sell shares or other securities in any other offering at a price per share that is less than the price per share paid by any investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into common stock, in future transactions may be higher or lower than the price per share paid by any investors in this offering.

We do not anticipate paying any cash dividends on our common stock in the foreseeable future. Accordingly, stockholders must rely on capital appreciation, if any, for any return on their investment.

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

The actual number of shares we will issue under the equity distribution agreement, at any one time or in total, is uncertain.

Subject to certain limitations in the equity distribution agreement and compliance with applicable law, we have the discretion to deliver a placement notice to Piper Sandler at any time throughout the term of the equity distribution agreement. The number of shares that are sold by Piper Sandler after delivering a placement notice will fluctuate based on the market price of our common stock during the sales period and limits we set with Piper Sandler. Because the price per share of each share sold will fluctuate based on the market price of our common stock during the sales period, it is not possible at this stage to predict the number of shares that will be ultimately issued.

The common stock offered hereby will be sold in “at the market offerings,” and investors who buy shares at different times will likely pay different prices.

Investors who purchase shares in this offering at different times will likely pay different prices, and so may experience different outcomes in their investment results. We will have discretion, subject to market demand, to vary the timing, prices, and numbers of shares sold. Investors may experience a decline in the value of their shares as a result of share sales made at prices lower than the prices they paid.

USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate gross sales proceeds of up to \$50,000,000 from time to time. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time.

We currently anticipate that we will use the net proceeds from this offering primarily for general corporate purposes, which may include working capital and capital expenditures, research and development expenses, including to fund clinical trials, regulatory submissions, commercialization, discovery and additional preclinical research and development of additional product candidates and platform enhancement, general and administrative expenses, and potential acquisitions of, or investments in, companies, technologies, products or assets that complement our business.

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

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

DILUTION

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

Our historical net tangible book value as of March 31, 2022 was approximately \$189.2 million, or \$4.65 per share of our common stock. Our historical net tangible book value is the amount of our total tangible assets less our total liabilities. Historical net tangible book value per share represents historical net tangible book value divided by the 40,684,025 shares of our common stock outstanding as of March 31, 2022, including 420 shares of unvested restricted stock awards subject to repurchase by us.

After giving effect to the assumed sale by us of shares of our common stock in the aggregate amount of \$50.0 million at an assumed public offering price of \$8.63 per share (the last sale price of our common stock on May 6, 2022 as reported on The Nasdaq Global Market), less the estimated commissions and estimated offering expenses payable by us, our as adjusted net tangible book value at March 31, 2022 would have been approximately \$237.5 million, or \$5.11 per share. This represents an immediate increase in as adjusted net tangible book value of \$0.46 per share to existing stockholders and an immediate dilution of \$3.52 per share to investors in this offering. The following table illustrates this per share dilution.

Assumed public offering price per share	\$8.63
Historical net tangible book value per share as of March 31, 2022	\$4.65
Increase in net tangible book value per share attributable to this offering	<u>0.46</u>
As adjusted net tangible book value per share after giving effect to this offering	<u>\$5.11</u>
Dilution per share to new investors purchasing shares in this offering	<u>\$3.52</u>

The as adjusted information is illustrative only and will adjust based on the actual price to the public, the actual number of shares sold and other terms of the offering determined at the time shares of our common stock are sold pursuant to this prospectus supplement. The as adjusted information assumes that all of our common stock in the aggregate amount of \$50.0 million is sold at the assumed offering price of \$8.63 per share, the last reported sale price of our common stock on The Nasdaq Global Market on May 6, 2022. The shares sold in this offering, if any, will be sold from time to time at various prices.

The table above excludes:

- 6,526,973 shares of common stock issuable upon exercise of stock options outstanding as of March 31, 2022 at a weighted average exercise price of \$13.85 per share;
- 44,427 shares of common stock issuable upon vesting of restricted stock units outstanding as of March 31, 2022; and
- 953,886, 1,718,480, and 1,113,021 shares of our common stock available for future issuance as of March 31, 2022 under our 2019 Stock Incentive Plan, our 2022 Inducement Stock Incentive Plan and our 2019 Employee Stock Purchase Plan, respectively, as well as any automatic increases in the number of shares of common stock reserved under these plans.

PLAN OF DISTRIBUTION

We have entered into the equity distribution agreement, dated May 9, 2022, with Piper Sandler, as our sales agent, pursuant to which we have agreed to issue and sell from time to time shares of our common stock having an aggregate offering price of \$50,000,000 through Piper Sandler.

This prospectus supplement only relates to \$50,000,000 of additional shares of our common stock that we may issue and sell from time to time under the equity distribution agreement. Unless otherwise indicated or the context otherwise requires, all references to the equity distribution agreement means the equity distribution agreement, dated May 9, 2022. We will be required to file another prospectus or prospectus supplement in the event we want to offer more than \$50,000,000 in shares of our common stock in accordance with the terms of the equity distribution agreement.

Piper Sandler will use commercially reasonable efforts to sell on our behalf all shares of our common stock requested to be sold by us, consistent with its normal trading and sales practices, under the terms and subject to the conditions set forth in the equity distribution agreement. We may instruct Piper Sandler not to sell our common stock if the sales cannot be effected at or above the price designated by us in any instruction. We or Piper Sandler may suspend the offering of our common stock upon proper notice and subject to other conditions, as further described in the equity distribution agreement.

Upon delivery of a placement notice, and subject to our instructions in that notice and the terms and conditions of the equity distribution agreement generally, Piper Sandler may sell our common stock by any method permitted by law that is deemed to be an “at the market offering” as defined in Rule 415(a)(4) promulgated under the Securities Act, including (A) in privately negotiated transactions; (B) as block transactions; or (C) by any other method permitted by law that is deemed to be an “at the market offering,” including sales made directly on or through The Nasdaq Global Market or on any other existing trading market for our common stock, in each case subject to our prior written consent. Piper Sandler will provide written confirmation to us no later than the opening of trading on The Nasdaq Global Market on the day following each day in which our common stock is sold under the equity distribution agreement. Each such confirmation will include the number of shares of our common stock sold on such day, the volume-weighted average price of the shares sold, the net proceeds to us and the compensation payable by us to Piper Sandler in connection with such sales.

We will pay Piper Sandler commissions for its services in acting as sales agent in the sale of our common stock. Piper Sandler will be entitled to compensation in an amount equal to 3.0% of the gross sales price of all common stock sold through it as sales agent under the equity distribution agreement. We have also agreed to reimburse Piper Sandler for the out-of-pocket reasonable fees and disbursements of its legal counsel, in an amount not to exceed \$50,000, and for FINRA-related expenses. We estimate that the total expenses for this offering, excluding compensation payable to Piper Sandler under the terms of the equity distribution agreement, will be approximately \$200,000.

Settlement for sales of our common stock will occur on the second business day following the date on which any such sales are made, or on some other date that is agreed upon by us and Piper Sandler in connection with a particular transaction, in return for payment of the net proceeds to us. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

We will report at least quarterly the number of shares of our common stock sold through Piper Sandler, as sales agent, under the equity distribution agreement, and the net proceeds to us in connection with such sales.

Piper Sandler and its affiliates have from time to time provided, and may in the future provide, various investment banking, commercial banking, fiduciary and advisory services for us for which they have

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received, and may in the future receive, customary fees and expenses. Piper Sandler and its affiliates may from time to time engage in other transactions with and perform services for us in the ordinary course of their business.

In connection with the sale of our common stock on our behalf, Piper Sandler will be deemed to be an underwriter within the meaning of the Securities Act, and the compensation paid by us to Piper Sandler will be deemed to be underwriting commissions or discounts. We have agreed to indemnify Piper Sandler against specified liabilities, including liabilities under the Securities Act, or to contribute to payments that Piper Sandler may be required to make because of such liabilities.

The offering of our common stock pursuant to the equity distribution agreement will terminate upon the earlier of (1) the sale of all common stock subject to equity distribution agreement or (2) termination of the equity distribution agreement. The equity distribution agreement may be terminated by Piper Sandler or us at any time upon specified prior written notice.

This summary of the material provisions of the equity distribution agreement does not purport to be a complete statement of its terms and conditions. A copy of the equity distribution agreement is filed as an exhibit to a current report on Form 8-K filed under the Exchange Act and incorporated by reference in this prospectus supplement.

LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon for us by Goodwin Procter LLP. Certain legal matters will be passed upon for Piper Sandler & Co. by Ropes & Gray LLP.

EXPERTS

The consolidated financial statements of Fulcrum Therapeutics, Inc. appearing in Fulcrum Therapeutics, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2021, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

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

This prospectus supplement is part of a registration statement we filed with the SEC. This prospectus supplement omits some information contained in the registration statement in accordance with SEC rules and regulations. You should review the information and exhibits in the registration statement for further information about us and our consolidated subsidiary and the securities we are offering. Statements in this prospectus supplement and the accompanying base 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 and the exhibits attached thereto. You should review the complete document to evaluate these statements. You can obtain a copy of the registration statement from the SEC's website.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to incorporate by reference much of the information we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus supplement and the accompanying base prospectus is considered to be part of this prospectus supplement. Because we are incorporating by reference future filings with the SEC, this prospectus supplement is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus supplement and the accompanying base prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus supplement or in any document previously incorporated by reference have been modified or superseded. This prospectus supplement 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 (in each case, other than those documents or the portions of those documents not deemed to be filed) until the offering of the securities offered hereby is terminated or completed:

- Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2021 filed on March 3, 2022.

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- Quarterly Report on Form 10-Q for the fiscal year ended March 31, 2022 filed on [May 9, 2022](#).
- the information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2021 from our definitive proxy statement on [Schedule 14A](#) (other than information furnished rather than filed) filed on April 28, 2022.
- Current Reports on Form 8-K filed on [January 4, 2022](#) (other than Item 2.02 and Item 9.01), [January 10, 2022](#) (other than Item 2.02 and Item 9.01) and [March 10, 2022](#).
- The description of our common stock contained in [Exhibit 4.2](#) to our Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2020 filed on March 4, 2021, and including any amendments and reports filed for the purpose of updating such description.

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

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

PROSPECTUS



\$250,000,000

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

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

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

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

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

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

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

The date of this prospectus is April 28, 2022

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ABOUT THIS PROSPECTUS

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

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

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

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

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

RISK FACTORS

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

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

WHERE YOU CAN FIND MORE INFORMATION

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

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

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

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

- Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2021 filed on March 3, 2022;
- Current Reports on Form 8-K filed on [January 4, 2022](#) and [January 10, 2022](#) (other than Item 2.02); and
- The description of our common stock contained in our registration statement on [Form 8-A](#) filed on July 12, 2019, as the description therein has been updated and superseded by the description of our capital stock contained in [Exhibit 4.2](#) to our Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2020, and including any amendments and reports filed for the purpose of updating such description.

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

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

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

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

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

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

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

ABOUT FULCRUM THERAPEUTICS, INC.

Overview

We are a clinical-stage biopharmaceutical company focused on improving the lives of patients with genetically defined rare diseases in areas of high unmet medical need. Our most advanced clinical product candidate, losmapimod, is in development to treat the root cause of facioscapulohumeral muscular dystrophy, or FSHD. Our other clinical product candidate is FTX-6058, which is being developed for the treatment of certain hemoglobinopathies, including sickle cell disease, or SCD, and β -thalassemia. We expect to initiate FSHD: REACH, a randomized, double-blind, placebo-controlled, multi-national Phase 3 clinical trial of losmapimod, our product candidate for FSHD, in the second quarter of 2022. We initiated a Phase 1b clinical trial of FTX-6058 in people with SCD in the fourth quarter of 2021, and we expect to report initial data from that Phase 1b trial in the second quarter of 2022. Additionally, we submitted an investigational new drug application, or IND, in the fourth quarter of 2021 for FTX-6058 in other select hemoglobinopathies, including β -thalassemia, and expect to initiate a Phase 1b study in the second quarter of 2022.

We have developed a proprietary product engine, FulcrumSeek, that we employ to systematically identify and validate cellular drug targets that can potentially modulate gene expression to treat known root causes of genetically defined diseases. Our product engine integrates patient-derived tissue and disease-relevant cell models that we interrogate using our pharmacologically diverse and highly annotated small-molecule compound library and customized CRISPR and RNAi libraries. These screens generate tens of millions of data points and high-content imaging. We then apply computational biology and analytics to identify targets with specificity and selectivity accompanied by a comprehensive data set that significantly accelerates development. This approach led to the identification of both losmapimod for FSHD and FTX-6058 for hemoglobinopathies, as well as a robust discovery pipeline. We expect to nominate our next development candidate this year to support our fourth IND by the end of the first quarter of 2023.

Corporate Information

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

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

USE OF PROCEEDS

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

DESCRIPTION OF DEBT SECURITIES

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

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

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

General

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

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

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

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

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- the price or prices at which we will sell the debt securities;
- the maturity date or dates of the debt securities and the right, if any, to extend such date or dates;
- the rate or rates, if any, at which the debt securities will bear interest, or the method of determining such rate or rates;
- the date or dates from which such interest will accrue, the interest payment dates on which such interest will be payable or the method of determination of such dates;
- the right, if any, to extend the interest payment periods and the duration of that extension;
- the manner of paying principal and interest and the place or places where principal and interest will be payable;
- the denominations of the debt securities if other than \$1,000 or multiples of \$1,000;
- provisions for a sinking fund, purchase fund or other analogous fund, if any;
- any redemption dates, prices, obligations and restrictions on the debt securities;
- the currency, currencies or currency units in which the debt securities will be denominated and the currency, currencies or currency units in which principal and interest, if any, on the debt securities may be payable;
- any conversion or exchange features of the debt securities;
- whether the debt securities will be subject to the defeasance provisions in the indenture;
- whether the debt securities will be issued in definitive or global form or in definitive form only upon satisfaction of certain conditions;
- whether the debt securities will be guaranteed as to payment or performance;
- any special tax implications of the debt securities;
- any events of defaults or covenants in addition to or in lieu of those set forth in the indenture; and
- any other material terms of the debt securities.

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

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

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

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

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

Certain Terms of the Senior Debt Securities

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Notice of Redemption. Notice of any redemption of senior debt securities will be mailed at least 10 days but not more than 60 days before the redemption date to each holder of senior debt securities of a series to be redeemed. Any notice may, at our discretion, be subject to the satisfaction or waiver of one or more conditions precedent. In that case, such notice shall state the nature of such condition precedent. If we elect to redeem a portion but not all of such senior debt securities, the trustee will select the senior debt securities to be redeemed in a method determined manner that complies with applicable legal and stock exchange requirements, if any. Interest on such debt securities or portions of senior debt securities will cease to accrue on and after the date fixed for redemption, unless we default in the payment of such redemption price and accrued interest with respect to any such senior debt security or portion thereof.

If any date of redemption of any senior debt security is not a business day, then payment of principal and interest may be made on the next succeeding business day with the same force and effect as if made on the nominal date of redemption and no interest will accrue for the period after such nominal date.

Conversion Rights. We will describe the terms upon which senior debt securities may be convertible into our common stock or other securities in a prospectus supplement. These terms will include the type of securities the senior debt securities are convertible into, the conversion price or manner of calculation thereof, the conversion period, provisions as to whether conversion will be at our option or the option of the holders, the events requiring an adjustment of the conversion price and provisions affecting conversion in the event of the redemption of the senior debt securities and any restrictions on conversion. They may also include provisions adjusting the number of shares of our common stock or other securities issuable upon conversion.

No Personal Liability of Incorporators, Stockholders, Officers or Directors. The senior indenture provides that no recourse shall be had under any obligation, covenant or agreement of ours in the senior indenture or any

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supplemental indenture, or in any of the senior debt securities or because of the creation of any indebtedness represented thereby, against any of our incorporators, stockholders, officers or directors, past, present or future, or of any predecessor or successor entity thereof under any law, statute or constitutional provision or by the enforcement of any assessment or by any legal or equitable proceeding or otherwise. Each holder, by accepting the senior debt securities, waives and releases all such liability.

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

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

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

Unclaimed Funds. All funds deposited with the trustee or any paying agent for the payment of principal, premium, interest or additional amounts in respect of the senior debt securities that remain unclaimed for two years after the date upon which such amounts became due and payable will be repaid to us. Thereafter, any right of any holder of senior debt securities to such funds shall be enforceable only against us, and the trustee and paying agents will have no liability therefor.

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

Certain Terms of the Subordinated Debt Securities

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

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

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

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

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

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

DESCRIPTION OF CAPITAL STOCK

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

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

As of December 31, 2021, we had issued and outstanding 40,636,398 shares of our common stock held by 33 stockholders of record (not including beneficial owners whose shares are held in “nominee” or “street” name), including 10,174 shares of unvested restricted stock subject to repurchase by us.

Common Stock

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

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

Preferred Stock

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

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

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

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

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

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

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

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

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

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

Different series of preferred stock may be entitled to dividends at different rates or based on different methods of calculation. The dividend rate may be fixed or variable or both. Dividends will be payable to the holders of

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record as they appear on our stock books on record dates fixed by our board of directors, as specified in the applicable prospectus supplement.

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

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

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

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

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

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

The prospectus supplement relating to a series of preferred stock that is subject to mandatory redemption will specify the number of shares of preferred stock that shall be redeemed by us in each year commencing after a date to be specified, at a redemption price per share to be specified, together with an amount equal to all accrued and unpaid dividends thereon to the date of redemption. Unless the shares have a cumulative dividend, such accrued dividends will not include any accumulation in respect of unpaid dividends for prior dividend periods.

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We may pay the redemption price in cash or other property, as specified in the applicable prospectus supplement. If the redemption price for preferred stock of any series is payable only from the net proceeds of the issuance of shares of our capital stock, the terms of such preferred stock may provide that, if no such shares of our capital stock shall have been issued or to the extent the net proceeds from any issuance are insufficient to pay in full the aggregate redemption price then due, such preferred stock shall automatically and mandatorily be converted into the applicable shares of our capital stock pursuant to conversion provisions specified in the applicable prospectus supplement. Notwithstanding the foregoing, we will not redeem any preferred stock of a series unless:

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

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

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

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

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

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

- the redemption date;
- the number of shares and series of preferred stock to be redeemed;
- the redemption price;
- the place or places where certificates for such preferred stock are to be surrendered for payment of the redemption price;
- that dividends on the shares to be redeemed will cease to accrue on such redemption date;
- the date on which the holder's conversion rights, if any, as to such shares shall terminate; and
- the specific number of shares to be redeemed from each such holder if fewer than all the shares of any series are to be redeemed.

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

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

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

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

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

Delaware Anti-Takeover Law and Certain Charter and Bylaw Provisions

Certain provisions of our certificate of incorporation, our bylaws and Delaware law may have the effect of making it more difficult for a third party to acquire, or of discouraging a third party from attempting to acquire, control of us. Such provisions could limit the price that certain investors might be willing to pay in the future for shares of our common stock and may limit the ability of stockholders to remove current management or directors or approve transactions that stockholders may deem to be in their best interest and, therefore, could adversely affect the price of our common stock.

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

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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 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

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of incorporation contains the choice of forum provision described above, it is possible that a court could rule that such a provision is inapplicable for a particular claim or action or that such provision is unenforceable.

Registration Rights

Investors' Rights Agreement

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

Demand and Form S-3 Registration Rights

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

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

Incidental Registration Rights

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

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

Expenses

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

The investors' rights agreement contains customary cross-indemnification provisions, pursuant to which we are obligated to indemnify the selling stockholders in the event of material misstatements or omissions in the

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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."

DESCRIPTION OF DEPOSITARY SHARES

General

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

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

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

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

Dividends and Other Distributions

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

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

Liquidation Preference

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

Withdrawal of Stock

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

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

Redemption of Depositary Shares

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

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

Voting the Preferred Stock

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

Charges of Depositary

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

Amendment and Termination of the Deposit Agreement

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

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

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

Resignation and Removal of Depositary

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

Notices

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

Limitation of Liability

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

DESCRIPTION OF UNITS

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

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

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

- the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities comprising the units may be traded separately;
- the identity of any unit agent for the units, if applicable, and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;
- any additional provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units;
- any applicable material U.S. federal income tax consequences; and
- any additional terms of the governing unit agreement, if applicable.

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

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

Unit Agent

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

Enforceability of Rights by Holders of Units

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

DESCRIPTION OF WARRANTS

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

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

FORMS OF SECURITIES

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

Global Securities

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

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

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

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

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

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

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

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

PLAN OF DISTRIBUTION

We may sell securities:

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Under Rule 15c6-1 of the Exchange Act, trades in the secondary market generally are required to settle in two business days, unless the parties to any such trade expressly agree otherwise. The applicable prospectus supplement may provide that the original issue date for your securities may be more than two scheduled business days after the trade date for your securities. Accordingly, in such a case, if you wish to trade securities on any date prior to the second business day before the original issue date for your securities, you will be

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required, by virtue of the fact that your securities initially are expected to settle in more than two scheduled business days after the trade date for your securities, to make alternative settlement arrangements to prevent a failed settlement.

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

LEGAL MATTERS

Unless the applicable prospectus supplement indicates otherwise, the validity of the securities in respect of which this prospectus is being delivered will be passed upon by Goodwin Procter 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, 2021 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.



\$50,000,000

Common Stock

Prospectus Supplement

Piper Sandler

May 9, 2022