

PROSPECTUS SUPPLEMENT
(To Prospectus dated April 25, 2024)**Fulcrum Therapeutics, Inc.****11,851,853 Shares of Common Stock****Pre-Funded Warrants to Purchase 1,111,193 Shares of Common Stock**

We are offering 11,851,853 of shares of our common stock pursuant to this prospectus supplement and accompanying prospectus, and, in lieu of common stock, pre-funded warrants to purchase 1,111,193 shares of our common stock, to certain investors.

Our common stock is traded on The Nasdaq Global Market under the symbol "FULC." On December 9, 2025, the last reported sale price per share of our common stock was \$14.60.

The purchase price of each pre-funded warrant will equal the price per share at which shares of our common stock are being sold to the public in this offering, minus \$0.001, which is the exercise price of each pre-funded warrant. The pre-funded warrants do not expire, and each pre-funded warrant will be exercisable at any time after the date of issuance, subject to an ownership limitation and in some cases clearance under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, or the HSR Act. This prospectus supplement also relates to the offering of the shares of our common stock issuable upon the exercise of such pre-funded warrants.

There is no established public trading market for the pre-funded warrants, and we do not expect a market to develop. We do not intend to list the pre-funded warrants on The Nasdaq Global Market or any other national securities exchange or nationally recognized trading system.

Investing in our securities involves a high degree of risk. You should carefully consider the risks and uncertainties described under the heading "[Risk Factors](#)" on page S-10 of this prospectus supplement and in the accompanying prospectus, as well as those contained in the other documents that are incorporated by reference into this prospectus supplement, the accompanying prospectus and any related free writing prospectus. You should carefully read this entire prospectus supplement and the accompanying prospectus, including any information incorporated by reference hereto and thereto, before deciding whether to purchase our securities.

	Per Share	Per Pre-Funded Warrant	Total
Public offering price	\$ 13.50	\$13.499	\$175,000,009.81
Underwriting discounts and commissions ⁽¹⁾	\$ 0.81	\$ 0.81	\$ 10,500,067.26
Proceeds to Fulcrum Therapeutics, Inc., before expenses	\$ 12.69	\$12.689	\$164,499,942.55

(1) See "Underwriting" beginning on page S-25 of this prospectus supplement for additional information regarding underwriting compensation.

The underwriters may also exercise their option to purchase up to an additional 1,944,456 shares of common stock from us, at the public offering price, less the underwriting discounts and commissions, for 30 days after the date of this prospectus supplement. If the underwriters exercise the option in full, the total underwriting discounts and commissions payable by us will be \$12.1 million, and the total proceeds to us, before expenses, will be \$189.2 million in each case, assuming no exercise of any pre-funded warrants offered or sold by us. See "Underwriting" for more information.

Neither the U.S. 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 prospectus. Any representation to the contrary is a criminal offense.

The shares of common stock and the pre-funded warrants will be ready for delivery against payment therefor on or about December 11, 2025.

*Book-Running Managers***J.P. Morgan****Leerink Partners****Cantor****Oppenheimer & Co.****Truist Securities**

Prospectus Supplement dated December 10, 2025

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ABOUT THIS PROSPECTUS SUPPLEMENT

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

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

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

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

Unless the context otherwise indicates, references in this prospectus supplement to “Fulcrum” “we,” “our,” “us” and “the Company” refer, collectively, to Fulcrum Therapeutics, Inc., a Delaware corporation and its consolidated subsidiary, and the term “securities” refers to shares of our common stock, pre-funded warrants and shares of common stock underlying the pre-funded warrants.

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.

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

- our ongoing clinical trial of pociredir, including the timing of data announcements and status of enrollment;
- the timing of and our ability to submit applications for, and obtain and maintain regulatory approvals for pociredir and any other product candidates;
- our expectations regarding our ability to fund our operating expenses and capital expenditure requirements with our cash, cash equivalents, and marketable securities;
- the initiation, timing, progress and results of our current and future preclinical studies and clinical trials (including planned investigational new drug application filings) and our research and development programs, including novel therapeutic agents for the potential treatment of bone marrow failure syndromes, such as Diamond-Blackfan anemia, or DBA, 5q deletion syndrome, Shwachman-Diamond syndrome, and Fanconi anemia, and other discovery programs;
- our plans to develop and, if approved, subsequently commercialize pociredir and any other product candidates, including in combination with other drugs and therapies;
- the potential advantages of our product candidates;
- the rate and degree of market acceptance and clinical utility of our products, if approved;
- our estimates regarding the potential market opportunity for our product candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- the initiation, timing, progress and results of our drug target discovery screening programs;
- our intellectual property position;
- the progress and results of our exclusive global license agreement with CAMP4 Therapeutics Corp.;
- our ability to identify, in-license, acquire or develop additional products, product candidates or technologies with significant commercial potential that are consistent with our commercial objectives;
- our estimates regarding expenses, future revenue, timing of any future revenue, capital requirements and needs for additional financing;

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- the impact of government laws and regulations, including uncertainty resulting from recent changes in the administration, shifts in government policy and the evolving regulatory environment;
- our competitive position;
- developments relating to our competitors and our industry;
- our ability to maintain and establish collaborations and license agreements or obtain additional funding;
- the impact of global pandemics or other geopolitical events or prolonged government shutdowns on our business and operations, including our clinical trials and development plans, as well as our future financial results;
- our expectations regarding the time during which we will be a smaller reporting company as defined under the federal securities laws; and
- our expectations regarding the completion of, and use of proceeds from, this offering.

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. Such forward looking statements are subject to various risks and uncertainties. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make.

You should also carefully review the "Risk Factors" in this prospectus supplement, along with the risk factors and cautionary statements described in the other documents incorporated by 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, collaborations, joint ventures or investments we may make or enter into.

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 SUPPLEMENT 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 securities discussed under "Risk Factors" beginning on page S-10 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, along with any free writing prospectus that we have authorized for use in connection with this offering.

Company Overview

We are a clinical-stage biopharmaceutical company focused on developing small molecules to improve the lives of patients with genetically defined rare diseases in areas of high unmet medical need. Our clinical-stage product candidate, pociredir, is being developed for the potential treatment of sickle cell disease, or SCD.

In addition, we developed a discovery approach 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 rare diseases. Our discovery approach led to the identification of pociredir for SCD, as well as other drug candidates. We continue to advance our program for the potential treatment of bone marrow failure syndromes, such as DBA, 5q deletion syndrome, Shwachman-Diamond syndrome, and Fanconi anemia, and we plan to submit an investigational new drug application, or IND, during the first half of 2026. We also presented preclinical data for FTX-6274, an oral embryonic ectoderm development, or EED, inhibitor candidate, at the European Society for Medical Oncology (ESMO) Congress 2025, demonstrating robust efficacy in castration resistant prostate cancer models.

Recent Developments

On December 6, 2025, we announced initial results from the ongoing 20 mg dose cohort (n=12) of the Phase 1b PIONEER trial of pociredir in SCD in connection with a presentation at the 67th American Society of Hematology Annual Meeting on such date. Results are as follows:

- Mean absolute fetal hemoglobin, or HbF, increased by 9.9% at 6 weeks of treatment with pociredir (vs. 5.6% at Week 6 and 8.6% at Week 12 in the 12 mg cohort), increasing from a baseline of 7.1% to 16.9%. As of the November 11, 2025 data cutoff, 7 of 12 patients (58%) achieved absolute HbF levels \geq 20% at Week 6, and all patients demonstrated a robust HbF increase. HbF levels of 20% are associated with ~90% of patients experiencing zero vaso-occlusive crises, or VOCs, per year, based on real-world data we presented at the 20th Annual Sickle Cell & Thalassemia Conference in October 2025.
- A clear dose-response was observed, with a >3.75-fold mean induction of HbF at Week 12 among patients who reached the Week 12 visit as of the November 11, 2025 data cutoff (n=6), compared to a 2.4-fold mean induction at Week 12 in the 12 mg cohort. The average baseline for these six patients is 5.0% as compared to 7.1% for the full cohort. Fold induction accounts for differences in baseline HbF levels and enables a normalized comparison of dose-response.
- The proportion of F-cells (HbF-containing red blood cells) increased from a mean of 31% at baseline to 58% at Week 6 (n=9), indicating early progression toward pan-cellular HbF induction (evenly distributed

across red blood cells). F-cells are resistant to sickling and hemolysis because of HbF-mediated inhibition of sickle hemoglobin (HbS) polymerization. Consequently, higher proportions of F-cells are associated with improved red blood cell health.

- Markers of hemolysis and erythropoiesis improved at Week 6:
 - Indirect bilirubin decreased by 37% (vs. 37% at Week 12 in the 12 mg cohort)
 - Lactate dehydrogenase decreased by 37% (vs. 28% at Week 12 in the 12 mg cohort)
 - Red cell distribution width decreased by 22% (vs. 27% at Week 12 in the 12 mg cohort)
 - Reticulocyte counts decreased by 33% (vs. 31% at Week 12 in the 12 mg cohort), indicating healthier bone marrow function
- Mean hemoglobin increased by 0.8 g/dL at Week 6 (vs. 0.9 g/dL at Week 12 in the 12 mg cohort), increasing from a baseline of 7.3 g/dL to 8.1 g/dL. Combined with reductions in reticulocyte counts, these findings indicate decreased red blood cell destruction and improvements in anemia.
- A trend of reduced VOC frequency was observed relative to patients' documented VOC frequency during the 6–12 months prior to enrollment. As of November 11, 2025 data cut off, eight of 12 patients (67%) reported no VOCs during the treatment period.

Pociredir Safety Update

- As of the November 11, 2025 data cutoff, pociredir has been dosed in 148 adults, including 89 subjects in multiple dose cohorts up to 12 weeks.
 - 103 healthy subjects, including 44 who received pociredir for 10 to 14 days treatment duration
 - 45 SCD patients who received pociredir for up to 12 weeks treatment duration
- The safety profile observed in the 20 mg dose cohort as of the November 11, 2025 data cutoff, together with follow-up data from the 12 mg dose cohort, remained consistent with previously reported safety data. Pociredir was generally well-tolerated, with no treatment-related serious adverse events and no discontinuations due to treatment-related adverse events as of the November 11, 2025, data cutoff.

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 to, or have applied for, 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 a Smaller Reporting Company

We are 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.

As long as we remain a smaller reporting company, we may continue to rely on exemptions from certain disclosure requirements that are applicable to public companies that are not smaller reporting companies. These scaled disclosure requirements include:

- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor’s report providing additional information about the audit and the financial statements; and
- reduced disclosure obligations regarding executive compensation.

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

THE OFFERING

Common stock offered by us pursuant to the prospectus supplement	11,851,853 shares of common stock
Pre-funded warrants offered by us pursuant to the prospectus supplement	<p>We are also offering, in lieu of common stock, pre-funded warrants to purchase up to 1,111,193 shares of our common stock to certain investors whose purchase of shares of common stock in this offering would otherwise result in such investor, together with its affiliates, beneficially owning shares of common stock with a value of or in excess of (i) the notification threshold of the HSR Act, or (ii) 4.99% (or, at the election of the purchaser, 9.99%) of the total number of shares of our common stock outstanding immediately after giving effect to such exercise. The purchase price of each pre-funded warrant will equal the price per share at which shares of common stock are being sold to the public in this offering, minus \$0.001, which is the exercise price of each pre-funded warrant. The pre-funded warrants do not expire, and each pre-funded warrant will be exercisable at any time after the date of issuance, subject to an ownership limitation and in some cases clearance under the HSR Act. See "Description of Pre-Funded Warrants" in this prospectus supplement for additional information. This prospectus supplement also relates to the offering of the shares of common stock issuable upon the exercise of such pre-funded warrants.</p>
Option to purchase additional shares	<p>The underwriters have a 30-day option to purchase up to an additional 1,944,456 of shares of common stock.</p>
Common stock to be outstanding immediately after this offering	<p>65,960,291 shares (67,904,747 shares if the underwriters exercise their option to purchase additional shares in full), in each case assuming no exercise of any pre-funded warrants offered and to be sold by us.</p>
Use of proceeds	<p>We estimate that the net proceeds to us from this offering will be approximately \$164.1 million, or approximately \$188.8 million if the underwriters exercise their option to purchase additional shares in full.</p> <p>We currently 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</p>

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 risks set forth under the caption “Item 1A. Risk Factors” included in our Quarterly Report on Form 10-Q for the three months ended September 30, 2025 and the other documents incorporated by reference into this prospectus supplement for a discussion of factors to consider carefully before deciding to purchase our securities.

Nasdaq Global Market Symbol

“FULC”. We do not intend to list the pre-funded warrants on The Nasdaq Global Market or any other national securities exchange or any recognized trading system. Without an active market, the liquidity of the pre-funded warrants will be limited.

The number of shares of our common stock shown above to be outstanding immediately after this offering is based on 54,108,438 shares of common stock outstanding as of September 30, 2025 and excludes the following:

- 11,870,785 shares of common stock issuable upon the exercise of stock options outstanding as of September 30, 2025 at a weighted average exercise price of \$6.57 per share;
- 69,486 shares of common stock issuable upon vesting of restricted stock units, or RSUs, outstanding as of September 30, 2025;
- 4,779,386, 1,681,184 and 2,052,030 shares of our common stock available for future issuance as of September 30, 2025 under our 2019 Stock Incentive Plan, or the 2019 Plan, our 2022 Inducement Stock Incentive Plan, or the Inducement Plan, and our 2019 Employee Stock Purchase Plan, or the ESPP, respectively, as well as any automatic increases in the number of shares of common stock reserved under these plans; and
- 8,500,000 shares of common stock issuable upon the exercise of pre-funded warrants outstanding as of September 30, 2025 at an exercise price of \$0.001 per share.

Unless otherwise indicated, all information in this prospectus supplement:

- assumes no exercise of the outstanding stock options, settlement of the RSUs or exercise of the outstanding pre-funded warrants described above;
- assumes no exercise by the underwriters of their option to purchase additional shares of our common stock in this offering;
- does not reflect the potential issuance of shares of our common stock that remain available for sale as of the date of this prospectus supplement under our “at-the-market” offering program, pursuant to which we may sell

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common stock for remaining gross proceeds of up to \$100 million from time to time under our Controlled Equity OfferingSM Sales Agreement with Cantor Fitzgerald & Co. and Stifel, Nicolas & Company, Incorporated; and

- assumes no exercise of the pre-funded warrants that we are offering in this offering in lieu of common stock to certain investors.

RISK FACTORS

Investing in our securities 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 Reports on Form 10-Q, 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. All of our outstanding shares of common stock are, and the shares of common stock (including shares of common stock underlying the pre-funded warrants) sold in this offering will be, freely tradeable without restriction or further registration under the Securities Act, unless owned or purchased by our "affiliates" as that term is defined in Rule 144 under 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 (including shares of common stock underlying the pre-funded warrants), or our ability to issue these shares of common stock, 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.

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

The price of the securities to be sold in this offering is substantially higher than the net tangible book value per share of our common stock. Therefore, if you purchase shares of our common stock (or pre-funded warrants in lieu thereof) in this offering, you will pay a price per share that substantially exceeds our net tangible book value per share after this offering. After giving effect to the sale of shares of our common stock and pre-funded warrants in the aggregate

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amount of 11,851,853 shares of our common stock and pre-funded warrants to purchase 1,111,193 shares of common stock at the public offering price of \$13.50 per share of common stock and \$13.499 per pre-funded warrant, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2025 would have been approximately \$362.5 million, or approximately \$5.50 per share. This represents an immediate increase in as adjusted net tangible book value of approximately \$1.83 per share to our existing stockholders and an immediate dilution in as adjusted net tangible book value of approximately \$8.00 per share to purchasers of our common stock or pre-funded warrants in this offering. See "Dilution" in this prospectus supplement for more information.

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

The trading price of our common stock has been, and is likely to continue to be, volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. During the period from July 18, 2019 to December 8, 2025, the closing price of our common stock ranged from a high of \$30.97 per share to a low of \$2.26 per share. The stock market in general and the market for smaller biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies.

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.

There is no public market for the pre-funded warrants being offered in this offering.

There is no public trading market for the pre-funded warrants being offered in this offering, and we do not expect a market to develop. In addition, we do not intend to list the pre-funded warrants on The Nasdaq Global Market or any other national securities exchange or nationally recognized trading system. Without an active trading market, the liquidity of the pre-funded warrants will be limited.

Except for the right to participate in certain dividends and distributions, holders of the pre-funded warrants will have no rights as common stockholders until such holders exercise their pre-funded warrants and acquire our common stock.

Until holders of the pre-funded warrants exercise their pre-funded warrants and acquire shares of our common stock, such holders will have no rights with respect to the shares of our common stock underlying such pre-funded warrants, except that the holder of a pre-funded warrant shall be entitled to participate in certain

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distributions, including cash dividends, if any, to all holders of our common stock for no consideration, subject to certain ownership limitations and in some cases clearance under the HSR Act. Upon exercise of the pre-funded warrants, the holders will be entitled to exercise the rights of a common stockholder only as to matters for which the record date occurs after the exercise date.

Significant holders or beneficial owners of our common stock may not be permitted to exercise the pre-funded warrants that they hold.

A holder of the pre-funded warrants will not be entitled to exercise any portion of any pre-funded warrant that, upon giving effect to such exercise, would cause (i) the aggregate number of shares of our common stock beneficially owned by such holder (together with its affiliates) to exceed 4.99% (or, at the election of the purchaser, 9.99%) of the number of shares of our common stock outstanding immediately after giving effect to the exercise; or (ii) the combined voting power of our securities beneficially owned by such holder (together with its affiliates) to exceed 4.99% (or, at the election of the purchaser, 9.99%) of the combined voting power of all of our securities outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the pre-funded warrants and subject to such holder's rights under the pre-funded warrants to increase or decrease such percentage to any other percentage not in excess of 19.99% upon at least 61 days' prior notice from the holder to us. In addition, where a holder notifies us that a filing under the HSR Act is required, we may not effect the exercise of any portion of any pre-funded warrant, and a holder will not be entitled to exercise any portion of any pre-funded warrant, which, upon giving effect to such exercise, would cause the aggregate number of shares of our common stock beneficially owned by the holder (together with its attribution parties) to equal or exceed the HSR Threshold (as defined below), until the applicable waiting period under the HSR Act has expired. As a result, you may not be able to exercise your pre-funded warrants for shares of our common stock at a time when it would be financially beneficial for you to do so. In such a circumstance, you could seek to sell your pre-funded warrants to realize value, but you may be unable to do so in the absence of an established trading market.

We will not receive any meaningful amount of additional funds upon the exercise of the pre-funded warrants.

Each pre-funded warrant will be exercisable until it is fully exercised and by means of payment of the nominal cash purchase price upon exercise or by means of a "cashless exercise" according to a formula set forth in the pre-funded warrant. Accordingly, we will not receive any meaningful additional funds upon the exercise of the pre-funded warrants.

DESCRIPTION OF PRE-FUNDED WARRANTS

The following is a brief summary of certain terms and conditions of the pre-funded warrants being offered. The following description is subject in all respects to the provisions contained in the pre-funded warrants.

Form

The pre-funded warrants will be issued as individual warrant agreements to investors. The form of pre-funded warrant will be filed as an exhibit to a Current Report on Form 8-K that we expect to file with the SEC.

Term

The pre-funded warrants do not expire.

Exercisability

The pre-funded warrants are exercisable at any time on or after their original issuance. The pre-funded warrants are exercisable, at the option of each holder, in whole or in part by delivering to us a duly executed exercise notice and by payment in full in immediately available funds for the number of shares of common stock purchased upon such exercise. As an alternative to payment in immediately available funds, the holder may, in its sole discretion, elect to exercise the pre-funded warrant through a cashless exercise, in which case the holder would receive upon such exercise the net number of shares of common stock determined according to the formula set forth in the pre-funded warrant. No fractional shares of common stock will be issued in connection with the exercise of a pre-funded warrant. In lieu of fractional shares, we will pay the holder an amount in cash equal to the fractional amount multiplied by the fair market value of the common stock on the exercise date.

Exercise Limitations

We may not effect the exercise of any pre-funded warrant, and a holder will not be entitled to exercise any portion of any pre-funded warrant that, upon giving effect to such exercise, would cause the aggregate number of shares of our common stock beneficially owned by the holder (together with its attribution affiliates (as defined below)) to exceed 4.99% (or, at the election of the purchaser, 9.99%) of the number of shares of our common stock that would be outstanding immediately after giving effect to the exercise. However, any holder of a pre-funded warrant may increase or decrease such percentage to any other percentage not in excess of 19.99% upon at least 61 days' prior notice from the holder to us. For purposes of the foregoing, "attribution affiliates" means, collectively, the following persons and entities with respect to any holder: (i) its direct or indirect affiliates, (ii) any person acting or who could be deemed to be acting as a Section 13(d) "group" together with the holder or any attribution parties and (iii) any other persons whose beneficial ownership of our common stock would or could be aggregated with the holder and/or any other attribution parties for purposes of Section 13(d) or Section 16 of the Exchange Act.

In addition, if the exercise of a pre-funded warrant would result in a holder of pre-funded warrants (together with its attribution affiliates) acquiring beneficial ownership of our common stock (together with all other equity owned by such holder at such time) equal to or in excess of the notification threshold applicable to the holder under the HSR Act as of the date of delivery of the applicable exercise notice, which we refer to as the HSR Threshold, and no exemption to filing a notice and report form under the HSR Act is applicable, then only such portion of the pre-funded warrants held by such holder, which when exercised does not exceed the HSR Threshold, shall be exercisable and the applicable exercise notice shall be deemed to relate only to such portion of the pre-funded warrants, and the remaining portion of the pre-funded warrants in excess of the HSR

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Threshold shall not be exercisable until the expiration or early termination of the applicable waiting period under the HSR Act or receipt of applicable approval.

Exercise Price

The exercise price per whole share of our common stock purchasable upon the exercise of the pre-funded warrants is \$0.001 per share of common stock. The exercise price of the pre-funded warrants is subject to appropriate adjustment in the event of certain stock dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting our common stock and also upon any distributions of assets, including cash, stock or other property to our stockholders.

Transferability

Subject to applicable laws, the pre-funded warrants may be offered for sale, sold, transferred or assigned without our consent. The ownership of the pre-funded warrants and any transfers of the pre-funded warrants will be registered in a warrant register maintained by the warrant agent. We will initially act as warrant agent.

Exchange Listing

There is no established trading market for the pre-funded warrants, and we do not expect a market to develop. We do not plan on applying to list the pre-funded warrants on The Nasdaq Global Market or any other national securities exchange or any nationally recognized trading system.

Fundamental Transactions

In the event of a fundamental transaction, as described in the pre-funded warrants and generally including any reorganization, recapitalization or reclassification of our common stock, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, the acquisition of more than 50% of our outstanding common stock, or any person or group becoming the beneficial owner of 50% of the voting power represented by our outstanding common stock, the holders of the pre-funded warrants will be entitled to receive upon exercise of the pre-funded warrants the kind and amount of securities, cash or other property that the holders would have received had they exercised the pre-funded warrants immediately prior to such fundamental transaction without regard to any limitations on exercise contained in the pre-funded warrants. In the event a holder does not exercise its pre-funded warrants in connection with a fundamental transaction, such holder's pre-funded warrants will be deemed exercised in full pursuant to the "cashless exercise" mechanic described above upon the consummation of such transaction.

Rights as a Stockholder

Except by virtue of such holder's ownership of shares of our common stock, the holder of a pre-funded warrant does not have the rights or privileges of a holder of our common stock, including any voting rights, until the holder exercises the pre-funded warrant. In the event of certain distributions, including cash dividends, if any, to all holders of our common stock for no consideration, the holder of a pre-funded warrant shall be entitled to participate in such distributions to the same extent as if such holder held the number of shares of our common stock acquirable upon complete exercise of its pre-funded warrant (without regard to any limitations on exercise). If such distribution would result in such holder and its affiliates to exceed the exercise limitations described above, a portion of such distribution shall be held in abeyance for the benefit of such holder until such time as the ownership limitations would not be exceeded.

USE OF PROCEEDS

We estimate that the net proceeds to us from the issuance and sale of shares of common stock (or pre-funded warrants in lieu thereof) in this offering will be approximately \$164.1 million, or approximately \$188.8 million if the underwriters exercise their option to purchase additional shares in full, in each case after deducting underwriting discounts and commissions and estimated offering expenses payable to us. We will receive nominal proceeds, if any, from any exercise of pre-funded warrants.

We currently anticipate that we will use the net proceeds from this offering, together with our existing cash, cash equivalents and marketable securities, 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, or pre-funded warrants in lieu thereof, in this offering, your ownership interest will be diluted immediately to the extent of the difference between the public offering price per share of our common stock or pre-funded warrants you will pay in this offering and the as adjusted net tangible book value per share of our common stock immediately after this offering.

Our historical net tangible book value as of September 30, 2025 was approximately \$198.4 million, or \$3.67 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 54,108,438 shares of our common stock outstanding as of September 30, 2025.

After giving effect to the issuance and sale of 11,851,853 shares of our common stock that we are offering at the public offering price of \$13.50 per share, and pre-funded warrants to purchase up to 1,111,193 shares of common stock at the public offering price of \$13.499 per pre-funded warrant (which equals the public offering price of the common stock at which shares of our common stock are being sold to the public in this offering less the \$0.001 per share exercise price of each such pre-funded warrant) (excluding shares of common stock issuable upon exercise of the pre-funded warrants, any proceeds which may be received upon exercise of the pre-funded warrants or any resulting accounting associated with the exercise of the pre-funded warrants), and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value at September 30, 2025 would have been approximately \$362.5 million, or \$5.50 per share. This represents an immediate increase in as adjusted net tangible book value of \$1.83 per share to existing stockholders and an immediate dilution of \$8.00 per share to investors in this offering. Dilution per share to new investors is determined by subtracting as adjusted net tangible book value per share after this offering from the public offering price per share paid by new investors. The following table illustrates this per share dilution.

Public offering price per share		\$ 13.50
Historical net tangible book value per share as of September 30, 2025	\$3.67	
Increase in net tangible book value per share attributable to this offering	\$1.83	
As adjusted net tangible book value per share after giving effect to this offering		\$ 5.50
Dilution per share to new investors purchasing shares in this offering		\$ 8.00

Assuming the pre-funded warrants were immediately and fully exercised, this would result in an as adjusted net tangible book value, after giving effect to this offering and pre-funded warrant exercise, of \$5.40 per share. This represents an increase in net tangible book value of \$1.73 per share to existing stockholders and dilution in net tangible book value per share of \$8.10 to new investors participating in this offering.

If the underwriters exercise their option to purchase additional shares in full, the immediate dilution in as adjusted net tangible book value per share to investors in this offering would be \$7.80 per share.

The table and discussion above are based on 54,108,438 shares of our common stock outstanding as of September 30, 2025, and exclude the following:

- 11,870,785 shares of common stock issuable upon the exercise of stock options outstanding as of September 30, 2025 at a weighted average exercise price of \$6.57 per share;
- 69,486 shares of common stock issuable upon vesting of RSUs outstanding as of September 30, 2025;

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- 4,779,386, 1,681,184 and 2,052,030 shares of our common stock available for future issuance as of September 30, 2025 under the 2019 Plan, the Inducement Plan and the ESPP, respectively, as well as any automatic increases in the number of shares of common stock reserved under these plans; and
- 8,500,000 shares of common stock issuable upon the exercise of pre-funded warrants outstanding as of September 30, 2025 at an exercise price of \$0.001 per share.

Further, the number of shares of our common stock to be outstanding after this offering does not take into account the 1,111,193 shares of our common stock issuable upon the exercise of the pre-funded warrants.

To the extent that outstanding stock options are exercised, outstanding RSUs are settled, outstanding or new pre-funded warrants are exercised, new stock options are issued, or we issue additional shares of common stock in the future, including pursuant to our Controlled Equity OfferingSM Agreement with Cantor Fitzgerald & Co. and Stifel, Nicolas & Company, Incorporated, there will be further dilution to investors purchasing securities in this offering.

MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS FOR INVESTORS IN COMMON STOCK AND PRE-FUNDED WARRANTS

The following summary describes the material U.S. federal income tax considerations applicable to the acquisition, ownership and disposition of our common stock and pre-funded warrants acquired in this offering. This discussion does not address all aspects of U.S. federal income taxes, does not discuss the potential application of the alternative minimum tax or Medicare Contribution tax and does not deal with state or local taxes, U.S. federal gift and estate tax laws or any non-U.S. tax consequences that may be relevant to investors in light of their particular circumstances.

Special rules different from those described below may apply to certain investors that are subject to special treatment under the Internal Revenue Code of 1986, as amended, or the Code, such as:

- insurance companies, banks and other financial institutions;
- tax-exempt organizations (including private foundations) and tax-qualified retirement plans;
- foreign governments and international organizations;
- broker-dealers and traders in securities;
- U.S. expatriates and former citizens or long-term residents of the United States;
- Non-U.S. Holders (as defined below) that own, or are deemed to own, more than 5% of our common stock (directly, indirectly or by attribution) or more than 5% of our pre-funded warrants;
- persons required for U.S. federal income tax purposes to conform the timing of income accruals to their financial statements under Section 451(b) of the Code;
- “controlled foreign corporations,” “passive foreign investment companies” and corporations that accumulate earnings to avoid U.S. federal income tax;
- persons that hold our common stock or pre-funded warrants as part of a “straddle,” “hedge,” “conversion transaction,” “synthetic security” or integrated investment or other risk reduction strategy;
- U.S. Holders (as defined below) whose functional currency for U.S. tax purposes is not the U.S. dollar;
- persons who do not hold our common stock or pre-funded warrants as “capital assets” within the meaning of Section 1221 of the Code (generally, for investment purposes); and
- partnerships and other pass-through entities, and investors in such pass-through entities (regardless of their places of organization or formation).

Such investors are urged to consult their own tax advisors to determine the U.S. federal, state, local and other tax consequences that may be relevant to them.

Furthermore, the discussion below is based upon the provisions of the Code, and Treasury regulations, rulings and judicial decisions thereunder as of the date hereof, and such authorities may be repealed, revoked or modified, possibly retroactively, and are subject to differing interpretations which could result in U.S. federal income tax consequences different from those discussed below. We have not requested a ruling from the Internal Revenue Service, or the IRS, with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS will agree with such statements and conclusions or will not take a contrary position regarding the tax consequences described herein, or that any such contrary position would not be sustained by a court.

For the purposes of this discussion, a “U.S. Holder” means a beneficial owner of our common stock or pre-funded warrants, other than a partnership or other pass-through entity, that is, for U.S. federal income tax purposes, (a) an individual citizen or resident of the United States, (b) a corporation (or other entity taxable as a corporation for U.S. federal income tax purposes), created or organized in or under the laws of the United States, any state thereof or the District of Columbia, (c) an estate the income of which is subject to U.S. federal income taxation regardless of its source, or (d) a trust if it (1) is subject to the primary supervision of a court within the United States and one or more “United States persons” (within the meaning of Section 7701(a)(30) of the Code) have the authority to control all substantial decisions of the trust or (2) has a valid election in effect under applicable U.S. Treasury regulations to be treated as a United States person.

If you are an individual non-U.S. citizen, you may, in some cases, be deemed to be a resident alien (as opposed to a nonresident alien) by virtue of being present in the United States for at least 31 days in the calendar year and for an aggregate of at least 183 days during a three-year period ending in the current calendar year. Generally, for this purpose, all the days present in the current year, one-third of the days present in the immediately preceding year, and one-sixth of the days present in the second preceding year, are counted.

Resident aliens are generally subject to U.S. federal income tax as if they were U.S. citizens. Individuals who are uncertain of their status as resident or nonresident aliens for U.S. federal income tax purposes are urged to consult their own tax advisors regarding the U.S. federal income tax consequences of the ownership or disposition of our common stock or pre-funded warrants.

PERSONS CONSIDERING THE PURCHASE OF OUR COMMON STOCK OR PRE-FUNDED WARRANTS PURSUANT TO THIS OFFERING SHOULD CONSULT THEIR OWN TAX ADVISORS CONCERNING THE U.S. FEDERAL INCOME TAX CONSEQUENCES OF ACQUIRING, OWNING AND DISPOSING OF OUR COMMON STOCK AND PRE-FUNDED WARRANTS IN LIGHT OF THEIR PARTICULAR SITUATIONS AS WELL AS ANY CONSEQUENCES ARISING UNDER THE LAWS OF ANY OTHER TAXING JURISDICTION, INCLUDING ANY STATE, LOCAL OR NON-U.S. TAX CONSEQUENCES OR ANY U.S. FEDERAL NON-INCOME TAX CONSEQUENCES, AND THE POSSIBLE APPLICATION OF TAX TREATIES.

Characterization of the Pre-Funded Warrants for Tax Purposes

Although the characterization of the pre-funded warrants for U.S. federal income tax purposes is not entirely clear, because the exercise price of the pre-funded warrants is a nominal amount, we expect to treat the pre-funded warrants as our common stock for U.S. federal income tax purposes and a holder of pre-funded warrants should generally be taxed in the same manner as a holder of common stock as described below. Accordingly, for U.S. federal income tax purposes, no gain or loss should be recognized upon the exercise of a pre-funded warrant, and upon exercise, the holding period of the share of common stock received should include the holding period of the pre-funded warrant. Similarly, the tax basis of a share of common stock received upon exercise of a pre-funded warrant should include the tax basis of the pre-funded warrant increased by the exercise price of \$0.001 per share. The balance of this discussion generally assumes that the characterization described above is respected for U.S. federal income tax purposes.

Our position with respect to the characterization of pre-funded warrants is not binding on the IRS and the IRS may treat the pre-funded warrants as warrants to acquire our common stock and, if so, the amount and character of your gain with respect to an investment in our pre-funded warrants could change. You should consult your tax advisor regarding the characterization of pre-funded warrants for U.S. federal income tax purposes, and the consequences to you of an investment in the pre-funded warrants based on your own particular facts and circumstances.

Tax Consequences to U.S. Holders

Distributions on Common Stock and Pre-funded Warrants

We do not expect to make distributions on our common stock (or pre-funded warrants) in the foreseeable future. In the event that we do make distributions of cash or other property, distributions paid on common stock (or pre-funded warrants) will be treated as a dividend to the extent paid out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles), and will be includible in your income as ordinary income when received. However, with respect to dividends received by individuals, such dividends are generally taxed at the lower applicable long-term capital gains rates, provided certain holding period requirements are satisfied. Distributions in excess of our current and accumulated earnings and profits will be treated as a return of capital to the extent of a U.S. Holder's tax basis in the common stock (or pre-funded warrant) and thereafter as capital gain from the sale or exchange of such common stock (or pre-funded warrant). The tax treatment of such gain is further described in "—Sale or Other Disposition of Common Stock or Pre-Funded Warrants" below. Dividends received by a corporation may be eligible for a dividends received deduction, subject to applicable limitations. Any such distributions will also be subject to the discussions below under the section titled "—Information Reporting and Backup Withholding."

A U.S. Holder of a pre-funded warrant is expected to receive any distributions paid with respect to common stock prior to the exercise of the pre-funded warrant and, in such case, would be taxed in the same manner as a U.S. Holder of common stock that receives such a distribution. However, under certain circumstances, it is possible for cash to be held in abeyance for the U.S. Holder until a pre-funded warrant is exercised or the ownership limitations (described under "Description of Pre-Funded Warrants") would not be exceeded, at which time such U.S. Holder shall be entitled to receive distributions. It is possible that such entitlement to distributions could cause the declaration of a distribution on our common stock to be currently taxable to U.S. Holders of pre-funded warrants, including under the principles governing Section 305 of the Code, even though the holders will not receive such distributions until a future date. Additionally, it is possible that other adjustments to the terms of the pre-funded warrant may be considered constructive distributions under Section 305 of the Code and taxable as discussed above. A holder of a pre-funded warrant should consult its tax advisor regarding the tax treatment of any distribution with respect to such pre-funded warrant that is held in abeyance in connection with any applicable limitation on the holder's beneficial ownership of our common stock.

Sale or Other Disposition of Common Stock or Pre-Funded Warrants

For U.S. federal income tax purposes, gain or loss realized on the sale or other disposition of common stock or pre-funded warrants will be capital gain or loss, and will be long-term capital gain or loss if you have held the common stock or pre-funded warrants for more than one year. The amount of the gain or loss will equal the difference between your tax basis in the common stock or pre-funded warrants disposed of and the amount realized on the disposition. Long-term capital gains recognized by non-corporate U.S. Holders will be subject to reduced tax rates. The deductibility of capital losses is subject to limitations.

Information Reporting and Backup Withholding

Information reporting requirements generally will apply to any payments of dividends on our common stock and pre-funded warrants, constructive dividends on our pre-funded warrants, and gross proceeds on the sale or other disposition of our common stock and pre-funded warrants, unless the U.S. Holder is an exempt recipient (such as a corporation). Backup withholding (currently at a 24% rate) will apply to those payments if the U.S. Holder fails to provide its correct taxpayer identification number, or certification of exempt status, or if the U.S. Holder is notified by the IRS that it has failed to report in full payments of interest and dividend income. Any

amounts withheld under the backup withholding rules will be allowed as a refund or a credit against a U.S. Holder's U.S. federal income tax liability provided the required information is furnished timely to the IRS.

Tax Consequences to Non-U.S. Holders

For purposes of this discussion, a Non-U.S. Holder is a beneficial owner of our common stock or pre-funded warrants, other than a partnership or other pass-through entity that is (i) a non-resident alien individual, (ii) a corporation or other foreign organization taxable as a corporation for U.S. federal income tax purposes that is created or organized in or under laws other than the laws of the United States, any state thereof, or the District of Columbia; (iii) an estate, the income of which is not subject to U.S. federal income tax on a net income basis; or (iv) a trust the income of which is not subject to U.S. federal income tax on a net income basis and that (1) has not made an election to be treated as a U.S. person under applicable U.S. Treasury Regulations and (2) either (i) is not subject to the primary supervision of a court within the United States or (ii) is not subject to the substantial control of one or more U.S. persons is not a U.S. Holder. If you are not a Non-U.S. Holder, this section does not apply to you.

Distributions on Common Stock and Pre-funded Warrants

We do not expect to make any distributions on our common stock (or pre-funded warrants) in the foreseeable future. If we do make distributions on our common stock (or pre-funded warrants), however, such distributions made to a Non-U.S. Holder will constitute dividends for U.S. tax purposes to the extent paid out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles). Distributions in excess of our current and accumulated earnings and profits will constitute a return of capital that is applied against and reduces, but not below zero, a Non-U.S. Holder's adjusted tax basis in our common stock (or pre-funded warrants). Any remaining excess will be treated as gain realized as described below under the section titled "—Sale or Other Disposition of Common Stock and Pre-Funded Warrants."

Any distribution on our common stock (or pre-funded warrants) that is treated as a dividend paid to a Non-U.S. Holder that is not effectively connected with the holder's conduct of a trade or business in the United States will generally be subject to withholding tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and the Non-U.S. Holder's country of residence. To obtain a reduced rate of withholding under a treaty, a Non-U.S. Holder generally will be required to provide the applicable withholding agent with a properly executed IRS Form W-8BEN, IRS Form W-8BEN-E or other appropriate form, certifying the Non-U.S. Holder's entitlement to benefits under that treaty. Such form must be provided prior to the payment of dividends and must be updated periodically. If a Non-U.S. Holder holds stock through a financial institution or other agent acting on the holder's behalf, the holder will be required to provide appropriate documentation to such agent. The holder's agent may then be required to provide certification to the applicable withholding agent, either directly or through other intermediaries. If you are eligible for a reduced rate of U.S. withholding tax under an income tax treaty, you should consult with your own tax advisor to determine if you are able to obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim with the IRS.

We generally are not required to withhold tax on dividends paid (or constructive dividends deemed paid) to a Non-U.S. Holder that are effectively connected with the holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, are attributable to a permanent establishment that the holder maintains in the United States) if a properly executed IRS Form W-8ECI, stating that the dividends are so connected, is furnished to us (or, if shares of our common stock are held through a financial institution or other agent, to the applicable withholding agent). In general, such effectively connected dividends will be subject to U.S. federal income tax on a net income basis at the regular graduated rates

applicable to U.S. persons, unless a specific treaty exemption applies. A corporate Non-U.S. Holder receiving effectively connected dividends may also be subject to an additional “branch profits tax,” which is imposed, under certain circumstances, at a rate of 30% (or such lower rate as may be specified by an applicable treaty) on the corporate Non-U.S. Holder’s effectively connected earnings and profits, subject to certain adjustments.

A Non-U.S. Holder of a pre-funded warrant is expected to receive any distributions paid with respect to common stock prior to the exercise of the pre-funded warrant and, in such case, would be taxed in the same manner as Non-U.S. Holder of common stock that receives such a distribution. However, under certain circumstances, it is possible for cash to be held in abeyance for a Non-U.S. Holder until a pre-funded warrant is exercised or the ownership limitations (described under “Description of Pre-Funded Warrants”) would not be exceeded, at which time the Non-U.S. Holder shall be entitled to receive distributions. It is possible that such entitlement to distributions could cause the declaration of a distribution on our common stock to be currently taxable to Non-U.S. Holders of pre-funded warrants, including under the principles governing Section 305 of the Code, even though such holders will not receive the distributions until a future date. Additionally, it is possible that other adjustments to the terms of the pre-funded warrant may be considered constructive distributions under Section 305 of the Code and taxable as discussed above. A holder of a pre-funded warrant should consult its tax advisor regarding the tax treatment of any distribution with respect to such pre-funded warrant that is held in abeyance in connection with any applicable limitation on the holder’s beneficial ownership of our common stock.

See also the section below titled “—Foreign Accounts” for additional withholding rules that may apply to dividends paid to certain foreign financial institutions or non-financial foreign entities.

Sale or Other Disposition of Common Stock and Pre-Funded Warrants

Subject to the discussion below under the sections titled “—Information Reporting and Backup Withholding” and “—Foreign Accounts,” a Non-U.S. Holder generally will not be subject to U.S. federal income or withholding tax with respect to gain realized on a sale or other disposition of our common stock or pre-funded warrants unless (a) the gain is effectively connected with a trade or business of the holder in the United States (and, if required by an applicable income tax treaty, is attributable to a permanent establishment that the holder maintains in the United States), (b) the Non-U.S. Holder is a nonresident alien individual and is present in the United States for a period or periods aggregating 183 or more days in the taxable year of the disposition and certain other conditions are met, or (c) we are or have been a “United States real property holding corporation” within the meaning of Code Section 897(c)(2), unless any class of our stock is regularly traded on an established securities market and the Non-U.S. Holder disposes of such class of stock and holds no more than 5% of such class of stock, directly or indirectly, actually or constructively, during the shorter of the 5-year period ending on the date of the disposition or the period that the Non-U.S. Holder held such class of stock.

If you are a Non-U.S. Holder described in (a) above, you will be required to pay tax on the net gain derived from the sale at the regular graduated U.S. federal income tax rates applicable to U.S. persons, unless a specific treaty exemption applies. Corporate Non-U.S. Holders described in (a) above may also be subject to the additional branch profits tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. If you are an individual Non-U.S. Holder described in (b) above, you will be required to pay a flat 30% tax on the gain derived from the sale, which gain may be offset by certain U.S. source capital losses (even though you are not considered a resident of the United States), provided you have timely filed U.S. federal income tax returns with respect to such losses. With respect to (c) above, in general, we would be a U.S. real property holding corporation if interests in U.S. real estate comprised (by fair market value) at least half of our worldwide real property interests plus our other assets used or held for use in a trade or business. We believe that we are not, and do not anticipate becoming, a U.S. real property holding corporation. However, there can be no assurance that we will not become a U.S. real property holding corporation in the future.

Information Reporting and Backup Withholding

Generally, we or certain financial middlemen must report information to the IRS with respect to any dividends we pay on our common stock or pre-funded warrants and any constructive dividends deemed paid on pre-funded warrants including the amount of any such dividends, the name and address of the recipient, and the amount, if any, of tax withheld. A similar report is sent to the holder to whom any such dividends are paid. Pursuant to tax treaties or certain other agreements, the IRS may make its reports available to tax authorities in the recipient's country of residence.

Dividends paid by us (or our paying agents) to a Non-U.S. Holder may also be subject to U.S. backup withholding. U.S. backup withholding generally will not apply to a Non-U.S. Holder who provides a properly executed IRS Form W-8BEN or IRS Form W-8BEN-E, as applicable, or otherwise establishes an exemption, provided that the applicable withholding agent does not have actual knowledge or reason to know the holder is a U.S. person.

Under current U.S. federal income tax law, U.S. information reporting and backup withholding requirements generally will apply to the proceeds of a disposition of our common stock or pre-funded warrants effected by or through a U.S. office of any broker, U.S. or non-U.S., unless the Non-U.S. Holder provides a properly executed IRS Form W-8BEN or IRS Form W-8BEN-E, as applicable, or otherwise meets documentary evidence requirements for establishing non-U.S. person status or otherwise establishes an exemption. Generally, U.S. information reporting and backup withholding requirements will not apply to a payment of disposition proceeds to a Non-U.S. Holder where the transaction is effected outside the United States through a non-U.S. office of a non-U.S. broker. Information reporting and backup withholding requirements may, however, apply to a payment of disposition proceeds if the broker has actual knowledge, or reason to know, that the holder is, in fact, a U.S. person. For information reporting purposes, certain brokers with substantial U.S. ownership or operations will generally be treated in a manner similar to U.S. brokers.

Backup withholding is not an additional tax. If backup withholding is applied to you, you should consult with your own tax advisor to determine whether you have overpaid your U.S. federal income tax, and whether you are able to obtain a tax refund or credit of the overpaid amount.

Foreign Accounts

In addition to, and separately from the withholding rules described above, U.S. federal withholding taxes may apply under the Foreign Account Tax Compliance Act, or FATCA, on certain types of payments, including dividends to non-U.S. financial institutions and certain other non-U.S. entities. Specifically, a 30% withholding tax may be imposed on dividends paid in respect of our common stock or pre-funded warrants, constructive distributions deemed paid with respect to pre-funded warrants and the gross proceeds of the disposition on our common stock or pre-funded warrants paid to a "foreign financial institution" or a "non-financial foreign entity" (each as defined in the Code), unless (1) the foreign financial institution agrees to undertake certain diligence and reporting obligations, (2) the non-financial foreign entity either certifies it does not have any "substantial United States owners" (as defined in the Code) or furnishes identifying information regarding each substantial United States owner, or (3) the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from these rules. The 30% federal withholding tax described in this paragraph cannot be reduced under an income tax treaty with the United States. If the payee is a foreign financial institution and is subject to the diligence and reporting requirements in (1) above, it must enter into an agreement with the U.S. Department of the Treasury requiring, among other things, that it undertake to identify accounts held by certain "specified United States persons" or "United States-owned foreign entities" (each as defined in the Code), annually report certain information about such accounts, and withhold 30% on certain payments to non-compliant foreign financial institutions and certain other account holders. Foreign financial

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institutions located in jurisdictions that have an intergovernmental agreement with the United States governing FATCA may be subject to different rules.

The Treasury Secretary has issued proposed regulations providing that the withholding provisions under FATCA do not apply with respect to payment of gross proceeds from a sale or other disposition of our common stock or pre-funded warrants, which may be relied upon by taxpayers until final regulations are issued. Prospective investors should consult their tax advisors regarding the potential application of withholding under FATCA to their investment in our common stock or pre-funded warrants.

EACH PROSPECTIVE INVESTOR SHOULD CONSULT ITS OWN TAX ADVISOR REGARDING THE TAX CONSEQUENCES OF PURCHASING, HOLDING AND DISPOSING OF OUR COMMON STOCK AND PRE-FUNDED WARRANTS, INCLUDING THE CONSEQUENCES OF ANY PROPOSED CHANGE IN APPLICABLE LAW, AS WELL AS TAX CONSEQUENCES ARISING UNDER ANY STATE, LOCAL, NON-U.S. OR U.S. FEDERAL NON-INCOME TAX LAWS SUCH AS ESTATE AND GIFT TAX.

UNDERWRITING

We are offering the securities described in this prospectus supplement through a number of underwriters. J.P. Morgan Securities LLC, Leerink Partners LLC and Cantor Fitzgerald & Co. are acting as joint book-running managers of the offering and as representatives of the underwriters. We have entered into an underwriting agreement with the representatives. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriters, and each underwriter has severally agreed to purchase, at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus supplement, the number of shares of common stock and pre-funded warrants listed next to its name in the following table:

Underwriters	Number of Shares	Number of Pre-Funded Warrants
J.P. Morgan Securities LLC	4,029,631	377,806
Leerink Partners LLC	3,437,037	322,246
Cantor Fitzgerald & Co.	2,607,408	244,462
Oppenheimer & Co. Inc.	1,066,666	100,007
Truist Securities, Inc.	711,111	66,672
Total	11,851,853	1,111,193

The underwriters are committed to purchase all the securities offered by us if they purchase any securities. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may also be increased or the offering may be terminated.

The underwriters propose to offer the securities directly to the public at the respective public offering prices set forth on the cover page of this prospectus supplement and to certain dealers at that price less a concession not in excess of \$0.486 per share of common stock or pre-funded warrant. After the offering of the securities to the public, if all of the securities are not sold at the respective public offering prices, the underwriters may change the offering price and the other selling terms. Sales of any securities made outside of the United States may be made by affiliates of the underwriters.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act.

Option to Purchase Additional Shares

The underwriters have an option to buy up to 1,944,456 additional shares of common stock from us to cover sales of shares by the underwriters which exceed the number of shares specified in the table above. The underwriters have 30 days from the date of this prospectus supplement to exercise this option to purchase additional shares. If any shares are purchased with this option to purchase additional shares, the underwriters will purchase shares in approximately the same proportion as shown in the table above. If any additional shares of common stock are purchased, the underwriters will offer the additional shares on the same terms as those on which the shares are being offered.

Commissions and Expenses

The underwriting fee is equal to the public offering price per share of common stock (or pre-funded warrant) less the amount paid by the underwriters to us per share of common stock (or pre-funded warrant). The underwriting fee is \$0.81 per share or pre-funded warrant. The following table shows the per share and

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pre-funded warrant and total underwriting discounts and commissions to be paid to the underwriters assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	Without option to purchase additional shares exercise	With full option to purchase additional shares exercise
Per Share	\$ 0.81	\$ 0.81
Per Pre-Funded Warrant	\$ 0.81	\$ 0.81
Total	\$ 10,500,067.26	\$ 12,075,076.62

We estimate that the total expenses of this offering, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding the underwriting discounts and commissions, will be approximately \$0.4 million.

Electronic Distribution

A prospectus supplement and accompanying prospectus in electronic format may be made available on the web sites maintained by one or more underwriters, or selling group members, if any, participating in the offering. The underwriters may agree to allocate a number of securities to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters and selling group members that may make Internet distributions on the same basis as other allocations.

No Sales of Similar Securities

We have agreed that we will not (i) offer, sell, contract to sell, pledge, grant any option to purchase, make any short sale or otherwise transfer or dispose of, directly or indirectly, or file with the SEC a registration statement under the Securities Act relating to, any of our securities that are substantially similar to the shares of common stock to be sold in this offering, including but not limited to any options or warrants to purchase shares of common stock or any securities that are convertible into or exchangeable for, or that represent the right to receive, common stock or any such substantially similar securities, or publicly disclose the intention to make any offer, sale, pledge, disposition or filing, or (ii) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of our common stock or any such other securities (regardless of whether any of these transactions are to be settled by delivery of common stock or such other securities, in cash or otherwise), in each case without the prior written consent of the representatives for a period of 60 days after the date of this prospectus supplement, other than the shares of our common stock to be sold in this offering.

The restrictions on our actions, as described above, do not apply to certain transactions, including (i) the securities to be sold hereunder, (ii) the issuance of shares of common stock or any securities (including without limitation options, restricted stock or restricted stock units) convertible into, or exercisable for, shares of our common stock pursuant to any employee stock option plan, incentive plan, stock plan, dividend reinvestment plan or otherwise in equity compensation arrangements existing as of the date of this prospectus supplement, (iii) the grant of awards pursuant to employee equity-based compensation plans, incentive plans, stock plans or other arrangements existing as of the date of this prospectus supplement, (iv) the filing of a registration statement on Form S-8 in connection with the registration of shares of common stock issuable under any employee equity-based compensation plan, incentive plan, stock plan, dividend reinvestment plan adopted and approved by our board of directors existing prior to the date of this prospectus supplement, or (v) the issuance

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of up to 5% of the outstanding shares of common stock immediately after the closing of this offering as in connection with the bona fide acquisition, strategic investment, licensing, commercialization, joint venture, technology transfer or development collaboration agreement with an unaffiliated third party; provided that in the case of (ii), (iii) and (v), all recipients of shares of common stock or any security convertible into or exercisable for common stock enter into a lock-up agreement with respect to the remaining portion of the 60-day lock-up period.

Our directors and executive officers, and certain stockholders (such persons, the "lock-up parties") have entered into lock-up agreements with the underwriters prior to the commencement of this offering pursuant to which each lock-up party, with limited exceptions, for a period of 30 days after the date of this prospectus supplement, may not (and may not cause any of their direct or indirect affiliates to), without the prior written consent of the representatives, (i) offer, sell, contract to sell, pledge, grant any option, right or warrant to purchase, purchase any option or contract to sell, lend or otherwise transfer or dispose of any shares of our common stock or any options or warrants to purchase shares of our common stock, or any securities convertible into or exercisable or exchangeable for or that represent the right to receive shares of our common stock, including, without limitation, common stock or such other securities which may be deemed to be beneficially owned by such lock-up parties in accordance with the rules and regulations of the SEC (such shares of common stock, options, rights, warrants or other securities, collectively, the "lock-up securities"), including without limitation any such lock-up securities now owned or hereafter acquired by the lock-up parties, (ii) engage in any hedging or other transaction or arrangement (including, without limitation, any short sale or the purchase or sale of, or entry into, any put or call option, or combination thereof, forward, swap or other derivative transaction or instrument, however described or defined) which is designed to or which reasonably could be expected to lead to or result in a sale, loan, pledge or other disposition (whether by the lock-up parties or someone other than the lock-up parties), or transfer any of the economic consequences of ownership, in whole or in part, directly or indirectly, of the lock-up securities, whether any such transaction or arrangement (or instrument provided for thereunder) would be settled by delivery of shares of common stock or other securities, in cash or otherwise (any such sale, loan, pledge or other disposition, or transfer of economic consequences, a "Transfer"), (iii) make any demand for, or exercise any right with respect to, the registration of any lock-up securities, or (iv) publicly disclose the intention to do any of the foregoing. The lock-up parties have further acknowledged that they have not, and have not caused or directed any of their affiliates to be or become, currently a party to any agreement or arrangement that provides for, is designed to or reasonably could be expected to lead to or result in any Transfer during the lock-up period.

The restrictions described in the immediately preceding paragraph and contained in the lock-up agreements between the underwriters and the lock-up parties do not apply, subject in certain cases to various conditions, to certain transactions, including transfers or dispositions of shares of common stock or any security convertible into or exercisable or exchangeable for common stock (a) as one or more bona fide gifts or charitable contributions, or for bona fide estate planning purposes; (b) upon death by will, testamentary document or intestate succession; (c) to any member of the immediate family of the lock-up party or to any trust for the direct or indirect benefit of the lock-up party or the immediate family of the lock-up party, if the lock-up party is a natural person or, if the lock-up party is a trust, to a trustor or beneficiary of the trust or the estate of a beneficiary of such trust; (d) to a partnership, limited liability company or other entity of which the lock-up party and their immediate family are the legal and beneficial owner of all of the outstanding equity securities or similar interests; (e) to a nominee or custodian of a person or entity to whom a disposition or transfer would be permissible under (a), (b), (c) or (d) above; (f) if the lock-up party is a corporation, partnership, limited liability company or other business entity (A) to another corporation, partnership, limited liability company or other business entity that is an affiliate of the lock-up party, or to any investment fund or other entity which fund or entity is controlled or managed by such lock-up party or affiliates of such lock-up party, or (B) as part of a distribution by the lock-up party to its stockholders, partners, members or other equityholders or to the estate

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of any such stockholders, partners, members or other equityholders; (g) by operation of law, such as pursuant to a qualified domestic order, divorce settlement, divorce decree or separation agreement; (h) by an employee to us upon the employee's death, disability or termination of employment; (i) in connection with the sale of the lock-up party's shares of common stock acquired from the underwriters in this offering or in open market transactions after the completion of this offering, if the lock-up party is not one of our officers or directors; and (j) to us in connection with the vesting, settlement or exercise of restricted stock units, options, warrants or other rights to purchase shares of our common stock (including, in each case, by way of "net" or "cashless" exercise) that are scheduled to expire or automatically vest during the lock-up period, including any transfer to us for the payment of tax withholdings or remittance payments due as a result of the vesting, settlement or exercise of such restricted stock units, options, warrants or other rights, or in connection with the conversion of convertible securities, in all such cases pursuant to equity awards granted under a stock incentive plan or other equity award plan, or pursuant to the terms of convertible securities, each as incorporated by reference into the registration statement of which this prospectus supplement forms a part; provided, however, that (1) in the case of clauses (a), (b), (c), (d), (e) and (f) above, such transfer or distribution shall not involve a disposition for value, (2) in the case of clauses (a), (b), (c), (d), (e), (f) and (g) above, it shall be a condition to the transfer or distribution that the donee, devisee, transferee or distributee, as the case may be, shall sign and deliver a lock-up agreement, (3) in the case of clauses (d), (e) and (f) above, no filing by any party (including, without limitation, any donor, donee, devisee, transferee or distributee) under the Exchange Act, or other public filing, report or announcement reporting a reduction in beneficial ownership of lock-up securities shall be required or shall be voluntarily made in connection with such transfer or distribution, and (4) in the case of clauses (a), (g), (h), (i) and (j) above, no filing under the Exchange Act or other public filing, report or announcement shall be voluntarily made, and if any such filing, report or announcement shall be legally required during the lock-up period, such filing, report or announcement shall clearly indicate in the footnotes thereto (x) the circumstances of such transfer or distribution and (y) in the case of a transfer or distribution pursuant to clauses (a) and (g) above, that the donee, devisee, transferee or distributee has agreed to be bound by a lock-up agreement.

The lock-up parties may (i) transfer, sell, or dispose of the lock-up securities pursuant to an existing Rule 10b5-1 trading plan adopted prior to the date of the lock-up agreement, which has not been amended following the date of the lock-up agreement, provided that any filing made under the Exchange Act in connection with such a sale shall disclose that the sale was made pursuant to a Rule 10b5-1 trading plan entered into on a date before the date of this prospectus supplement and (ii) enter into a written plan meeting the requirements of Rule 10b5-1 under the Exchange Act relating to the transfer, sale or other disposition of the lock-up parties' lock-up securities, if then permitted by us, provided that (a) none of the securities subject to such plan may be transferred, sold or otherwise disposed of until after the expiration of the lock-up period and (b) to the extent a public announcement or filing under the Exchange Act, if any, is required by or on behalf of the lock-up parties or us regarding the entry of such plan, such announcement or filing shall include a statement to the effect that no transfer of shares of common stock may be made under such plan during the lock-up period.

The lock-up parties may also transfer lock-up securities pursuant to a bona fide third-party tender offer, merger, consolidation or other similar transaction that is approved by our board and made to all holders of our capital stock involving a change of control; provided that in the event that such tender offer, merger, consolidation or other similar transaction is not completed, the lock-up parties' lock-up securities shall remain subject to the provisions of the lock-up agreement.

The representatives, in their sole discretion, may release the securities subject to any of the lock-up agreements with the underwriters described above, in whole or in part at any time.

Listing

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

Stabilization

In connection with this offering, the underwriters may engage in stabilizing transactions, which involves making bids for, purchasing and selling shares of common stock in the open market for the purpose of preventing or retarding a decline in the market price of the common stock while this offering is in progress. These stabilizing transactions may include making short sales of common stock, which involves the sale by the underwriters of a greater number of shares of common stock than they are required to purchase in this offering, and purchasing shares of common stock on the open market to cover positions created by short sales. Short sales may be “covered” shorts, which are short positions in an amount not greater than the underwriters’ option to purchase additional shares referred to above, or may be “naked” shorts, which are short positions in excess of that amount. The underwriters may close out any covered short position either by exercising their option to purchase additional shares, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriters will consider, among other things, the price of shares available for purchase in the open market compared to the price at which the underwriters may purchase shares through the option to purchase additional shares. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market that could adversely affect investors who purchase in this offering. To the extent that the underwriters create a naked short position, they will purchase shares in the open market to cover the position.

The underwriters have advised us that, pursuant to Regulation M of the Securities Act, they may also engage in other activities that stabilize, maintain or otherwise affect the price of the common stock, including the imposition of penalty bids. This means that if the representatives of the underwriters purchase common stock in the open market in stabilizing transactions or to cover short sales, the representatives can require the underwriters that sold those shares as part of this offering to repay the underwriting discount received by them.

These activities may have the effect of raising or maintaining the market price of the common stock or preventing or retarding a decline in the market price of the common stock, and, as a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue them at any time. The underwriters may carry out these transactions on the Nasdaq Global Select Market, in the over-the-counter market or otherwise.

Other Activities and Relationships

Certain of the underwriters and their affiliates have provided in the past to us and our affiliates and may provide from time to time in the future certain commercial banking, financial advisory, investment banking and other services for us and such affiliates in the ordinary course of their business, for which they have received and may continue to receive customary fees and commissions. In addition, from time to time, certain of the underwriters and their affiliates may effect transactions for their own account or the account of customers, and hold on behalf of themselves or their customers, long or short positions in our debt or equity securities or loans, and may do so in the future.

Selling Restrictions

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus supplement in any jurisdiction where action for that purpose is required. The securities offered by this prospectus supplement may not be offered or sold, directly or indirectly, nor may this prospectus supplement or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except

under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus supplement comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus supplement. This prospectus supplement does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus in any jurisdiction in which such an offer or a solicitation is unlawful.

Notice to Prospective Investors in the European Economic Area

In relation to each Member State of the European Economic Area (each, a "Member State"), no securities have been offered or will be offered pursuant to the offering to the public in that Member State prior to the publication of a prospectus in relation to the securities which has been approved by the competent authority in that Member State, all in accordance with the Prospectus Regulation, except that offers of securities may be made to the public in that Member State at any time under the following exemptions under the Prospectus Regulation:

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

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

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

Notice to Prospective Investors in the United Kingdom

In relation to the United Kingdom, no securities have been offered or will be offered pursuant to the offering to the public in the United Kingdom prior to the publication of a prospectus in relation to the securities which has been approved by the Financial Conduct Authority, or (ii) is to be treated as if it had been approved by the Financial Conduct Authority in accordance with the transitional provision in Regulation 74 of the Prospectus (Amendment etc.) (EU Exit) Regulations 2019, except that offers of securities may be made to the public in the United Kingdom of any securities at any time under the following exemptions under the UK Prospectus Regulation:

- to any legal entity which is a qualified investor as defined under Article 2 of the UK Prospectus Regulation;
- to fewer than 150 natural or legal persons (other than qualified investors as defined under Article 2 of the UK Prospectus Regulation), subject to obtaining the prior consent of the representatives for any such offer; or
- in any other circumstances falling within Section 86 of the FSMA,

provided that no such offer of the securities shall require the Company or any of the underwriters to publish a prospectus pursuant to Section 85 of the FSMA or supplement a prospectus pursuant to Article 23 of the UK Prospectus Regulation.

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For the purposes of this provision, the expression an “offer to the public” in relation to the securities in the United Kingdom means the communication in any form and by any means of sufficient information on the terms of the offer and any securities to be offered so as to enable an investor to decide to purchase or subscribe for any securities and the expression “UK Prospectus Regulation” means Regulation (EU) 2017/1129 as it forms part of domestic law by virtue of the European Union (Withdrawal) Act 2018.

In addition, this prospectus supplement and the accompanying prospectus are only being distributed to, and is only directed at, and any investment or investment activity to which this prospectus supplement and the accompanying prospectus relate is available only to, and will be engaged in only with, persons who are outside the United Kingdom or persons in the United Kingdom (i) having professional experience in matters relating to investments who fall within the definition of “investment professionals” in Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, or the Order; or (ii) who are high net worth entities falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as “relevant persons”). Persons who are not relevant persons should not take any action on the basis of this prospectus supplement and the accompanying prospectus and should not act or rely on them.

Notice to Prospective Investors in Hong Kong

No securities have been offered or sold, and no securities may be offered or sold, in Hong Kong, by means of any document, other than: (i) to persons whose ordinary business is to buy or sell shares or debentures, whether as principal or agent; or (ii) to “professional investors” as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong (the “SFO”) and any rules made under that Ordinance; or in other circumstances which do not result in the document being a “prospectus” as defined in the Companies Ordinance (Cap. 32) of Hong Kong (the “CO”) or which do not constitute an offer or invitation to the public for the purpose of the CO or the SFO. No document, invitation or advertisement relating to the securities has been issued or may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), that is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted under the securities laws of Hong Kong) other than with respect to securities that are or are intended to be disposed of only to persons outside Hong Kong or only to “professional investors” as defined in the SFO and any rules made under that Ordinance.

This prospectus supplement and the accompanying prospectus have not been registered with the Registrar of Companies in Hong Kong. Accordingly, this prospectus supplement and the accompanying prospectus may not be issued, circulated or distributed in Hong Kong, and the securities may not be offered for subscription to members of the public in Hong Kong. Each person acquiring the securities will be required, and is deemed by the acquisition of the securities, to confirm that he is aware of the restriction on offers of the securities described in this prospectus supplement and accompanying prospectus and that he is not acquiring, and has not been offered, any securities in circumstances that contravene any such restrictions.

Notice to Prospective Investors in Japan

The offering has not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948 of Japan, as amended, the “FIEL”) and the underwriters will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (the term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with the FIEL and any other applicable laws, regulations and ministerial guidelines of Japan.

Notice to Prospective Investors in Singapore

This prospectus supplement and the accompanying prospectus have not been and will not be lodged or registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and the accompanying prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the securities offered hereby may not be circulated or distributed, nor may the securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than: (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the "SFA"); (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275, of the SFA; or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the securities are subscribed or purchased under Section 275 of the SFA by a relevant person that is:

- a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)), the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor); or
- a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor, securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the securities pursuant to an offer made under Section 275 of the SFA except:
- to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;
- where no consideration is or will be given for the transfer;
- where the transfer is by operation of law;
- as specified in Section 276(7) of the SFA; or
- as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

Notice to Prospective Investors in Canada

Resale Restrictions

The offering of the securities in Canada is being made only in the provinces of Ontario, Quebec, Alberta and British Columbia on a private placement basis exempt from the requirement that we prepare and file a prospectus with the securities regulatory authorities in each province where trades of these securities are made. Any resale of the securities in Canada must be made under applicable securities laws which may vary depending on the relevant jurisdiction and which may require resales to be made under available statutory exemptions or under a discretionary exemption granted by the applicable Canadian securities regulatory authority. Purchasers are advised to seek legal advice prior to any resale of the securities.

Representations of Canadian Purchasers

By purchasing the securities in Canada and accepting delivery of a purchase confirmation, a purchaser is representing to us and the dealer from whom the purchase confirmation is received that:

- the purchaser is entitled under applicable provincial securities laws to purchase the securities without the benefit of a prospectus qualified under those securities laws, as it is an “accredited investor” as defined under National Instrument 45-106—*Prospectus Exemptions*;
- the purchaser is a “permitted client” as defined under National Instrument 31-103—*Registration Requirements, Exemptions and Ongoing Registrant Obligations*;
- where required by law, the purchaser is purchasing as principal and not as agent; and
- the purchaser has reviewed the text above under “Resale Restrictions.”

Conflicts of Interest

Canadian purchasers are hereby notified that the underwriters relying on the exemption set out in section 3A.3 or 3A.4, if applicable, of National Instrument 33-105—*Underwriting Conflicts*, to not provide certain conflict of interest disclosures in this document.

Statutory Rights of Action

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if the offering memorandum (including any amendment thereto) such as this document contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser’s province or territory. The purchaser of these securities in Canada should refer to any applicable provisions of the securities legislation of the purchaser’s province or territory for particulars of these rights or consult with a legal advisor.

Enforcement of Legal Rights

All of our directors and officers as well as the experts named herein may be located outside of Canada, and, as a result, it may not be possible for Canadian purchasers to effect service of process within Canada upon us or those persons. All or a substantial portion of our assets, and the assets of those persons may be located outside of Canada, and, as a result, it may not be possible to satisfy a judgment against us or those persons in Canada or to enforce a judgment obtained in Canadian courts against us or those persons outside of Canada.

Taxation and Eligibility for Investment

Canadian purchasers of the securities should consult their own legal and tax advisors with respect to the tax consequences of an investment in the securities in their particular circumstances and about the eligibility of the securities for investment by the purchaser under relevant Canadian legislation.

Notice to Prospective Investors in Australia

This prospectus supplement and the accompanying prospectus is not a disclosure document for the purposes of Australia’s Corporations Act 2001 (Cth) of Australia (the “Corporations Act”), has not been lodged with the Australian Securities and Investments Commission and is only directed to the categories of exempt persons set

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out below. Accordingly, if you receive this prospectus supplement and the accompanying prospectus in Australia, you confirm and warrant that you are either:

- a “sophisticated investor” under Section 708(8)(a) or (b) of the Corporations Act;
- a “sophisticated investor” under Section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant’s certificate to the Company that complies with the requirements of Section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made;
- a person associated with the Company under Section 708(12) of the Corporations Act; or
- a “professional investor” under Section 708(11)(a) or (b) of the Corporations Act.

To the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor, associated person or professional investor under the Corporations Act, any offer made to you under this prospectus supplement and the accompanying prospectus is void and incapable of acceptance.

Further, you warrant and agree that you will not offer any of the securities issued to you pursuant to this prospectus supplement and the accompanying prospectus for resale in Australia within 12 months of those securities being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under Section 708 of the Corporations Act.

Notice to Prospective Investors in Israel

This document does not constitute a prospectus under the Israeli Securities Law, 5728-1968 (the “Israeli Securities Law”), and has not been filed with or approved by the Israel Securities Authority. In Israel, this prospectus supplement and the accompanying prospectus is being distributed only to, and is directed only at, and any offer of the securities offered hereby is directed only at: (i) a limited number of persons in accordance with the Israeli Securities Law; and (ii) investors listed in the first addendum to the Israeli Securities Law, as it may be amended from time to time (the “Addendum”), consisting primarily of joint investment in trust funds, provident funds, insurance companies, banks, portfolio managers, investment advisors, members of the Tel Aviv Stock Exchange, underwriters, venture capital funds, entities with equity in excess of NIS 50 million and “qualified individuals,” each as defined in the Addendum, collectively referred to as qualified investors (in each case, purchasing for their own account or, where permitted under the Addendum, for the accounts of their clients who are investors listed in the Addendum). Qualified investors are required to submit written confirmation that they fall within the scope of the Addendum, are aware of the meaning of the Addendum and agree to it.

Notice to Prospective Investors in Switzerland

The securities may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange (“SIX”) or on any other stock exchange or regulated trading facility in Switzerland. This prospectus supplement and the accompanying prospectus has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this prospectus supplement and the accompanying prospectus, nor any other offering or marketing material relating to the securities or the offering, may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this prospectus supplement and the accompanying prospectus, nor any other offering or marketing material relating to the offering, the Company or the securities offered hereby, have been or will be filed with

or approved by any Swiss regulatory authority. In particular, this prospectus supplement and the accompanying prospectus will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, and the offer of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes (the "CISA"). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of the securities offered hereby.

Notice to Prospective Investors in the United Arab Emirates

The securities have not been, and are not being, publicly offered, sold, promoted or advertised in the United Arab Emirates (including the Dubai International Financial Centre ("DIFC")) other than in compliance with the laws of the United Arab Emirates (and the DIFC) governing the issue, offering and sale of securities. Further, this prospectus supplement and the accompanying prospectus do not constitute a public offer of securities in the United Arab Emirates (including the DIFC) and is not intended to be a public offer. This prospectus supplement and the accompanying prospectus have not been approved by or filed with the Central Bank of the United Arab Emirates, the Securities and Commodities Authority, Financial Services Regulatory Authority or the Dubai Financial Services Authority.

Notice to Prospective Investors in Saudi Arabia

This document may not be distributed in the Kingdom of Saudi Arabia except to such persons as are permitted under the Rules on the Offer of Securities and Continuing Obligations Regulations as issued by the board of the Saudi Arabian Capital Market Authority ("CMA"), pursuant to resolution number 3-123-2017 dated 27 December 2017, as amended. The CMA does not make any representation as to the accuracy or completeness of this document and expressly disclaims any liability whatsoever for any loss arising from, or incurred in reliance upon, any part of this document. Prospective purchasers of the securities offered hereby should conduct their own due diligence on the accuracy of the information relating to the securities. If you do not understand the contents of this document, you should consult an authorized financial adviser

LEGAL MATTERS

The validity of the securities offered hereby will be passed upon by Goodwin Procter LLP, Boston, Massachusetts. Mintz, Levin, Cohn, Ferris, Glovsky, and Popeo, P.C., Boston, Massachusetts, is acting as counsel for the underwriters in connection with certain legal matters relating to this offering.

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, 2024 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 until the offering of securities offered hereby is terminated or completed (in each case, other than those documents or the portions deemed to have been “furnished” and not filed with the SEC, including those made pursuant to Item 2.02, Item 7.01 or Item 9.01 of Form 8-K or other information):

- Annual Report on Form 10-K for the year ended December 31, 2024, filed on February 25, 2025, including the information specifically incorporated by reference into our Annual Report on [Form 10-K](#) from our definitive proxy statement on [Schedule 14A](#) (other than information furnished rather than filed) filed on April 30, 2025;
- Quarterly Reports on Form 10-Q for the quarters ended March 31, 2025, June 30, 2025 and September 30, 2025, filed on [May 1, 2025](#), [July 29, 2025](#) and [October 29, 2025](#), respectively;
- Current Reports on Form 8-K filed on [March 4, 2025](#), [June 27, 2025](#), [July 29, 2025](#) (other than information furnished rather than filed), and [December 8, 2025](#); and
- The description of our common stock contained in our registration statement on [Form 8-A](#) filed on July 12, 2019, as 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 in 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



\$350,000,000
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 \$350,000,000. 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 and sell these securities in amounts, at prices and on terms determined at the time of offering and which will be set forth in a prospectus supplement to this prospectus and any related free writing prospectus. 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". On February 26, 2024, the closing price for our common stock, as reported on The Nasdaq Global Market, was \$9.73 per share.

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 25, 2024

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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 \$350,000,000.

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 our most recent Quarterly Report on Form 10-Q, as well as 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, 2023 filed on February 27, 2024; 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 developing small molecules to improve the lives of patients with genetically defined rare diseases in areas of high unmet medical need. Our most advanced clinical-stage product candidate, losmapimod, is being developed for the potential treatment of facioscapulohumeral muscular dystrophy, or FSHD. Our other clinical-stage product candidate is pociredir, formerly known as FTX-6058, which is being developed for the potential treatment of sickle cell disease, or SCD. We initiated REACH, a randomized, double-blind, placebo-controlled, multi-national Phase 3 clinical trial of losmapimod in the second quarter of 2022 and we completed enrollment during September 2023. The trial enrolled 260 patients. We expect to report topline data from REACH in the fourth quarter of 2024.

In January 2023, we announced interim data from our Phase 1b clinical trial of pociredir in SCD. We completed enrollment in the 6 mg and 2 mg dose cohorts, and we do not plan to enroll additional subjects in these cohorts. Although we commenced enrollment in the 12 mg dose cohort, in February 2023 the U.S. Food and Drug Administration placed a full clinical hold on the Investigational New Drug application for pociredir for SCD, which was lifted in August 2023. The Phase 1b clinical trial is being re-initiated at the 12 mg once daily dose level, with that cohort expected to enroll approximately 10 patients, and will be followed by an additional cohort of approximately 10 patients at the 20 mg once daily dose level. Following the clinical hold, we amended the protocol to revise the inclusion and exclusion criteria for the Phase 1b clinical trial to target patients with higher disease severity.

In addition to product candidate development, we have developed a drug discovery approach 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 rare diseases. Our discovery approach led to the identification of both losmapimod for FSHD and pociredir for SCD, as well as a robust discovery pipeline.

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 and potential acquisition of, or investment in, companies, technologies, products or assets that complement our business. 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. Each series of debt securities may have different terms. 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. Together, the senior indenture and the subordinated indenture are referred to as the indentures and, together, the senior trustee and the subordinated trustee are referred to as the trustees. This prospectus briefly outlines some of the provisions of the indentures. The following summary of the material provisions of the indentures is qualified in its entirety by the provisions of the indentures, including definitions of certain terms used in the indentures. Wherever we refer to particular sections or defined terms of 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. As used in this prospectus, the term “debt securities” includes the debt securities being offered by this prospectus and all other debt securities issued by us under the indentures.

General

The indentures:

- do not limit the amount of debt securities that we may issue;
- allow us to issue debt securities in one or more series;
- do not require us to issue all of the debt securities of a series at the same time; and
- allow us to reopen a series to issue additional debt securities without the consent of the holders of the debt securities of such series.

Unless otherwise provided in the applicable prospectus supplement, the senior debt securities will be unsubordinated obligations and will rank equally with all of our other unsecured and unsubordinated indebtedness. Payments on the subordinated debt securities will be subordinated to the prior payment in full of all of our senior indebtedness, as described under “—Subordination” and in the applicable prospectus supplement.

Each indenture provides that we may, but need not, designate more than one trustee under an indenture. Any trustee under an indenture may resign or be removed and a successor trustee may be appointed to act with respect to the series of debt securities administered by the resigning or removed trustee. If two or more persons are acting as trustee with respect to different series of debt securities, each trustee shall be a trustee of a trust under the applicable indenture separate and apart from the trust administered by any other trustee. Except as otherwise indicated in this prospectus, any action described in this prospectus to be taken by each trustee may be taken by each trustee with respect to, and only with respect to, the one or more series of debt securities for which it is trustee under the applicable indenture.

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The prospectus supplement for each offering will provide the following terms, where applicable:

- the title of the debt securities and whether they are senior or subordinated;
- any limit upon the aggregate principal amount of the debt securities of that series;
- the date or dates on which the principal of the debt securities of the series is payable;
- the price at which the debt securities will be issued, expressed as a percentage of the principal and, if other than the principal amount thereof, the portion of the principal amount thereof payable upon declaration of acceleration of the maturity thereof or, if applicable, the portion of the principal amount of such debt securities that is convertible into another security of ours or the method by which any such portion shall be determined;
- the rate or rates at which the debt securities of the series shall bear interest or the manner of calculation of such rate or rates, if any;
- the date or dates from which interest will accrue, the interest payment dates on which such interest will be payable or the manner of determination of such interest payment dates, the place(s) of payment, and the record date for the determination of holders to whom interest is payable on any such interest payment dates or the manner of determination of such record dates;
- the right, if any, to extend the interest payment periods and the duration of such extension;
- the period or periods within which, the price or prices at which and the terms and conditions upon which debt securities of the series may be redeemed, converted or exchanged, in whole or in part;
- our obligation, if any, to redeem or purchase debt securities of the series pursuant to any sinking fund, mandatory redemption, or analogous provisions (including payments made in cash in satisfaction of future sinking fund obligations) or at the option of a holder thereof and the period or periods within which, the price or prices at which, and the terms and conditions upon which, debt securities of the series shall be redeemed or purchased, in whole or in part, pursuant to such obligation;
- the form of the debt securities of the series including the form of the Certificate of Authentication for such series;
- if other than minimum denominations of one thousand U.S. dollars (\$1,000) or any integral multiple of \$1,000 thereof, the denominations in which the debt securities of the series shall be issuable;
- whether the debt securities of the series shall be issued in whole or in part in the form of a global debt security or global debt securities; the terms and conditions, if any, upon which such global debt security or global debt securities may be exchanged in whole or in part for other individual debt securities; and the depositary for such global debt security or global debt securities;
- whether the debt securities will be convertible into or exchangeable for common stock or other securities of ours or any other Person and, if so, the terms and conditions upon which such debt securities will be so convertible or exchangeable, including the conversion or exchange price, as applicable, or how it will be calculated and may be adjusted, any mandatory or optional (at our option or the holders' option) conversion or exchange features, and the applicable conversion or exchange period;
- any additional or alternative events of default to those set forth in the indenture;
- any additional or alternative covenants to those set forth in the indenture;
- the currency or currencies including composite currencies, in which payment of the principal of (and premium, if any) and interest, if any, on such debt securities shall be payable (if other than the currency of the United States of America), which unless otherwise specified shall be the currency of the United States of America as at the time of payment is legal tender for payment of public or private debts;

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- if the principal of (and premium, if any), or interest, if any, on such debt securities is to be payable, at our election or at the election of any holder thereof, in a coin or currency other than that in which such debt securities are stated to be payable, then the period or periods within which, and the terms and conditions upon which, such election may be made;
- whether interest will be payable in cash or additional debt securities at our or the holders' option and the terms and conditions upon which the election may be made;
- the terms and conditions, if any, upon which we will pay amounts in addition to the stated interest, premium, if any and principal amounts of the debt securities of the series to any holder that is not a "United States person" for federal tax purposes;
- additional or alternative provisions, if any, related to defeasance and discharge of the offered debt securities than those set forth in the indenture;
- the applicability of any guarantees;
- any restrictions on transfer, sale or assignment of the debt securities of the series; and
- any other terms of the debt securities (which may supplement, modify or delete any provision of the indenture insofar as it applies to such series).

We may issue debt securities that provide for less than the entire principal amount thereof to be payable upon declaration of acceleration of the maturity of the debt securities. We refer to any such debt securities throughout this prospectus as "original issue discount securities."

We will provide you with more information in the applicable prospectus supplement regarding any deletions, modifications, or additions to the events of default or covenants that are described below, including any addition of a covenant or other provision providing event risk or similar protection.

Payment

Unless otherwise provided in the applicable prospectus supplement, the principal of, and any premium or make-whole amount, and interest on, any series of the debt securities will be payable by mailing a check to the address of the person entitled to it as it appears in the applicable register for the debt securities or by wire transfer of funds to that person at an account maintained within the United States.

All monies that we pay to a paying agent or a trustee for the payment of the principal of, and any premium, or interest on, any debt security will be repaid to us if unclaimed at the end of two years after the obligation underlying payment becomes due and payable. After funds have been returned to us, the holder of the debt security may look only to us for payment, without payment of interest for the period which we hold the funds.

Merger, Consolidation or Sale of Assets

The indentures provide that we may, without the consent of the holders of any outstanding debt securities, (i) consolidate with, (ii) sell, lease or convey all or substantially all of our assets to, or (iii) merge with or into, any other entity provided that:

- either we are the continuing entity, or the successor entity, if other than us, assumes the obligations (a) to pay the principal of, and any premium, and interest on, all of the debt securities and (b) to duly perform and observe all of the covenants and conditions contained in the applicable indenture; and in the event the debt securities are convertible into or exchangeable for common stock or other securities of ours, such successor entity will, by such supplemental indenture, make provision so that the holders of debt securities of that series shall thereafter be entitled to receive upon conversion or exchange of such debt securities the number of securities or property to which a holder of the number of common

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stock or other securities of ours deliverable upon conversion or exchange of those debt securities would have been entitled had such conversion or exchange occurred immediately prior to such consolidation, merger, sale, conveyance, transfer or other disposition; and

- an officers' certificate and legal opinion covering such conditions are delivered to each applicable trustee.

Events of Default, Notice and Waiver

Unless the applicable prospectus supplement states otherwise, when we refer to "events of default" as defined in the indentures with respect to any series of debt securities, we mean:

- default in the payment of any installment of interest on any debt security of such series continuing for 90 days unless such date has been extended or deferred;
- default in the payment of principal of, or any premium on, any debt security of such series when due and payable unless such date has been extended or deferred;
- default in the performance or breach of any covenant or warranty in the debt securities or in the indenture by us continuing for 90 days after written notice described below;
- bankruptcy, insolvency or reorganization, or court appointment of a receiver, liquidator or trustee of us; and
- any other event of default provided with respect to a particular series of debt securities.

If an event of default (other than an event of default described in the fourth bullet point above) occurs and is continuing with respect to debt securities of any series outstanding, then the applicable trustee or the holders of 25% or more in principal amount of the debt securities of that series will have the right to declare the principal amount of, and accrued interest on, all the debt securities of that series to be due and payable. If an event of default described in the fourth bullet point above occurs, the principal amount of, and accrued interest on, all the debt securities of that series will automatically become and will be immediately due and payable without any declaration or other act on the part of the trustee or the holders of the debt securities. However, at any time after such a declaration of acceleration has been made, but before a judgment or decree for payment of the money due has been obtained by the applicable trustee, the holders of at least a majority in principal amount of outstanding debt securities of such series or of all debt securities then outstanding under the applicable indenture may rescind and annul such declaration and its consequences if:

- we have deposited with the applicable trustee all required payments of the principal, any premium, interest and, to the extent permitted by law, interest on overdue installment of interest, plus applicable fees, expenses, disbursements and advances of the applicable trustee; and
- all events of default, other than the non-payment of accelerated principal, or a specified portion thereof, and any premium, have been cured or waived.

The indentures provide that holders of debt securities of any series may not institute any proceedings, judicial or otherwise, with respect to such indenture or for any remedy under the indenture, unless the trustee fails to act for a period of 90 days after the trustee has received a written request to institute proceedings in respect of an event of default from the holders of 25% or more in principal amount of the outstanding debt securities of such series, as well as an offer of indemnity reasonably satisfactory to the trustee. However, this provision will not prevent any holder of debt securities from instituting suit for the enforcement of payment of the principal of, and any premium, and interest on, such debt securities at the respective due dates thereof.

The indentures provide that, subject to provisions in each indenture relating to its duties in the case of a default, a trustee has no obligation to exercise any of its rights or powers at the request or direction of any holders of any

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series of debt securities then outstanding under the indenture, unless the holders have offered to the trustee reasonable security or indemnity. The holders of at least a majority in principal amount of the outstanding debt securities of any series or of all debt securities then outstanding under an indenture shall have the right to direct the time, method and place of conducting any proceeding for any remedy available to the applicable trustee, or of exercising any trust or power conferred upon such trustee. However, a trustee may refuse to follow any direction which:

- is in conflict with any law or the applicable indenture;
- may involve the trustee in personal liability; or
- may be unduly prejudicial to the holders of debt securities of the series not joining the proceeding.

Within 120 days after the close of each fiscal year, we will be required to deliver to each trustee a certificate, signed by one of our several specified officers, stating whether or not that officer has knowledge of any event of default under the applicable indenture. If the officer has knowledge of any event of default, the notice must specify the nature and status of the default.

Modification of the Indentures

Subject to certain exceptions, the indentures may be amended with the consent of the holders of a majority in aggregate principal amount of the outstanding debt securities of all series affected by such amendment (including consents obtained in connection with a tender offer or exchange for the debt securities of such series).

However, subject to the terms of the indenture for any series of debt securities that we may issue or as otherwise provided in the prospectus supplement or free writing prospectus applicable to a particular series of debt securities, we and the trustee may make the following changes only with the consent of each holder of any outstanding debt securities affected:

- extending the stated maturity of the series of debt securities;
- reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption or repurchase of any debt securities; or
- reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

We and the applicable trustee may make modifications and amendments of an indenture without the consent of any holder of debt securities for any of the following purposes:

- to cure any ambiguity, defect, or inconsistency in the applicable indenture or in the Securities of any series;
- to comply with the covenant described above under “—Merger, Consolidation or Sale of Assets”;
- to provide for uncertificated debt securities in addition to or in place of certificated debt securities;
- to add the covenants, restrictions, conditions or provisions relating to us for the benefit of the holders of all or any series of debt securities (and if such covenants, restrictions, conditions or provisions are to be for the benefit of less than all series of debt securities, stating that such covenants, restrictions, conditions or provisions are expressly being included solely for the benefit of such series), to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default, or to surrender any right or power in the applicable indenture conferred upon us;
- to add to, delete from, or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication, and delivery of debt securities, as set forth in the applicable indenture;

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- to make any change that does not adversely affect the rights of any holder of notes under the applicable indenture in any material respect;
- to provide for the issuance of and establish the form and terms and conditions of the debt securities of any series as provided in the applicable indenture, to establish the form of any certifications required to be furnished pursuant to the terms of the applicable indenture or any series of debt securities under the applicable indenture, or to add to the rights of the holders of any series of debt securities;
- to evidence and provide for the acceptance of appointment under the applicable indenture by a successor trustee or to appoint a separate trustee with respect to any series; or
- to comply with any requirements of the SEC or any successor in connection with the qualification of the indenture under the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act.

Subordination

Payment by us of the principal of, premium, if any, and interest on any series of subordinated debt securities issued under the subordinated indenture will be subordinated to the extent set forth in an indenture supplemental to the subordinated indenture relating to such series.

Discharge, Defeasance and Covenant Defeasance

Unless otherwise provided in the applicable prospectus supplement, the indentures allow us to discharge our obligations (except for certain specified obligations) to holders of any series of debt securities issued under any indenture when:

- either (i) all securities of such series have already been delivered to the applicable trustee for cancellation; or (ii) all securities of such series have not already been delivered to the applicable trustee for cancellation but (a) have become due and payable, (b) will become due and payable within one year, or (c) if redeemable at our option, are to be redeemed within one year, and we have irrevocably deposited with the applicable trustee, in trust, funds in such currency or currencies, or governmental obligations in an amount sufficient to pay the entire indebtedness on such debt securities in respect of principal and any premium, and interest to the date of such deposit if such debt securities have become due and payable or, if they have not, to the stated maturity or redemption date; and
- we have paid or caused to be paid all other sums payable.

Unless otherwise provided in the applicable prospectus supplement, the indentures provide that, upon our irrevocable deposit with the applicable trustee, in trust, of an amount, in such currency or currencies in which such debt securities are payable at stated maturity, or government obligations, or both, applicable to such debt securities, which through the scheduled payment of principal and interest in accordance with their terms will provide money in an amount sufficient to pay the principal of, and any premium or make-whole amount, and interest on, such debt securities, and any mandatory sinking fund or analogous payments thereon, on the scheduled due dates therefor, the issuing company shall be released from its obligations (except for certain specified obligations) with respect to such debt securities under the applicable indenture or, if provided in the applicable prospectus supplement, its obligations with respect to any other covenant, and any omission to comply with such obligations shall not constitute an event of default with respect to such debt securities.

The applicable prospectus supplement may further describe the provisions, if any, permitting such defeasance or covenant defeasance, including any modifications to the provisions described above, with respect to the debt securities of or within a particular series.

Conversion Rights

The terms and conditions, if any, upon which the debt securities are convertible into common stock or other securities of ours will be set forth in the applicable prospectus supplement. The terms will include whether the

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debt securities are convertible into shares of common stock or other securities of ours, the conversion price, or manner of calculation thereof, the conversion period, provisions as to whether conversion will be at the issuing company's 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 debt securities and any restrictions on conversion.

Governing Law

The indentures and the debt securities will be governed by and construed in accordance with the laws of the State of New York, except to the extent that the Trust Indenture Act is applicable.

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, as amended, 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.

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.

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;

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- 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 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

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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. 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

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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.

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.

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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 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

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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, the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction. Although our certificate of incorporation contains the choice of forum provision described above, it is possible that a court could rule that such a provision is inapplicable for a particular claim or action or that such provision is unenforceable.

Transfer Agent and Registrar

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

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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, 2023 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.



11,851,853 Shares of Common Stock

Pre-Funded Warrants to Purchase 1,111,193 Shares of Common Stock

PROSPECTUS SUPPLEMENT

Book-Running Managers

J.P. Morgan

Leerink Partners

Cantor

Oppenheimer & Co.

Truist Securities

December 10, 2025