Filed Pursuant to Rule 424(b)(5)
Registration No. 333-291348

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

Subject to Completion, dated November 10, 2026

PRELIMINARY PROSPECTUS SUPPLEMENT
(To Prospectus dated March 3, 2026)

$125,000,000

prime_ medicine

Common Stock

We are offering $125,000,000 of shares of our common stock.

Our common stock is listed on The Nasdaq Global Market under the symbol "PRME." On November 9, 2026, the closing price of our common stock, as reported on The Nasdaq Global Market, was $4.30 per share.

Investing in shares of our common stock involves risks that are described in the "Risk Factors" section beginning on page S-9 of this prospectus supplement and page 1 of the accompanying prospectus, and in the other documents that are incorporated by reference herein. You should read the entire prospectus supplement and the accompanying prospectus, including any information incorporated by reference herein or therein, carefully before you make your investment decision.

We are an "emerging growth company" and "smaller reporting company" under the federal securities laws and, as such, are subject to reduced public company reporting requirements. See "Prospectus Supplement Summary — Implications of Being an Emerging Growth Company and Smaller Reporting Company."

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

(1) We refer you to "Underwriting" for additional information regarding underwriting compensation.

We have granted the underwriters an option to purchase up to an additional $18,750,000 of shares of our common stock from us, at the public offering price, less underwriting discounts and commissions, within 30 days of the date of this prospectus supplement.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement and the accompanying prospectus are truthful or complete. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares to purchasers on or about , 2026.

Joint Book-Running Managers

Jefferies **TD Cowen** **Goldman Sachs & Co. LLC**

Passive Book-Running Managers

Oppenheimer & Co. **LifeSci Capital**

The date of this prospectus supplement is , 2026.

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We have not and the underwriters have not authorized anyone to provide you with any information other than the information contained in this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein and therein, and any free writing prospectus we have authorized for use in connection with this offering. We take no responsibility for, and can provide no assurances as to the reliability of, any information that is in addition to or different from that contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. You should not assume that the information contained in this prospectus supplement and the accompanying prospectus, or in any free writing prospectus that we have authorized for use in connection with this offering, is accurate as of any date other than the date of

those respective documents, or that information contained in any document incorporated by reference is accurate as of any date other than the date of the document incorporated by reference. Our business, financial condition, liquidity, results of operations and prospects may have changed since those dates. We are not, and the underwriters are not, making offers to sell these securities in any jurisdiction in which an offer or solicitation is not authorized or permitted or in which the person making such offer or solicitation is not qualified to do so or to any person to whom it is unlawful to make such an offer or solicitation. You should read this prospectus supplement, the accompanying prospectus, including any information incorporated by reference, and any free writing prospectus that we have authorized for use in connection with this offering, in their entirety before making an investment decision. You should also read and consider the information in the documents to which we have referred you in the sections entitled “Incorporation of Certain Information by Reference” and “Where You Can Find More Information.”

ABOUT THIS PROSPECTUS SUPPLEMENT

This document is part of the registration statement that we filed with the Securities and Exchange Commission (the "SEC") using a "shelf" registration process, and consists of two parts. The first part is this prospectus supplement, including the documents incorporated by reference herein, which describes the specific terms of this offering. The second part, the accompanying prospectus, including the documents incorporated by reference therein, gives more general information, some of which may not apply to this offering. Generally, when we refer to the "prospectus," we are referring to both parts combined. This prospectus supplement and any free writing prospectus we authorize for use in connection with this offering may add to, update or change information in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement or the accompanying prospectus.

If information in this prospectus supplement is inconsistent with the accompanying prospectus or with any document incorporated by reference herein or therein that was filed with the SEC before the date of this prospectus supplement, you should rely on the information contained 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, the statement in the document having the later date modifies or supersedes the earlier statement. This prospectus supplement, the accompanying prospectus, the documents incorporated by reference into each and any free writing prospectus we authorize for use in connection with this offering include important information about us, the shares and other information you should consider before purchasing the shares. See the sections entitled "Incorporation of Certain Information by Reference" and "Where You Can Find More Information" in this prospectus supplement.

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 and 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.

As used in this prospectus supplement or the accompanying prospectus, unless the context otherwise requires, references to the terms "Prime," "Prime Medicine," "the Company," "we," "us," and "our" and similar designations refer to Prime Medicine, Inc. and, where appropriate, our wholly-owned subsidiary.

We intend to apply for various trademarks that we use in connection with the operation of our business. This prospectus supplement may also contain trademarks, service marks and trade names of third parties, which are the property of their respective owners. Our use or display of third parties' trademarks, service marks, trade names or products in this prospectus supplement is not intended to, and does not imply a relationship with, or endorsement or sponsorship by us. Solely for convenience, the trademarks, service marks and trade names referred to in this prospectus supplement may appear without the ®, SM and ™ symbols, but the omission of such references is not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the right of the applicable owner of these trademarks, service marks and trade names.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the accompanying prospectus, including the documents that we incorporate by reference, include forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). All statements, other than statements of historical fact, contained herein, including statements regarding our plans, objectives and expectations for our business, operations and financial performance and condition, can be identified by terminology such as "anticipate," "believe," "contemplate," "continue," "could," "estimate," "expect," "goal," "hope," "intend," "may," "might," "plan," "possible," "potential," "predict," "project," "seek," "should," "strategy," "target," "will," "would," "can," "future" or the negative of these words or other similar expressions. Forward-looking statements are based on management's beliefs and assumptions and on information currently available to management. Although we believe that the expectations reflected in forward-looking statements are reasonable, such statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by forward-looking statements.

These forward-looking statements include, but are not limited to, statements about:

- the initiation, timing, progress and results of our research and development programs, product candidates, and ongoing and future preclinical studies and future clinical trials;
- our ability to demonstrate, and the timing of, preclinical proof-of-concept *in vivo* for multiple programs;
- our ability to advance our current product candidates and any future product candidates that we may identify and successfully complete any clinical trials, including the manufacture of any such product candidates;
- our ability to pursue our areas of focus and any other additional programs we may advance;
- our ability to quickly leverage programs within our initial target indications and to progress additional programs to further develop our pipeline;
- the timing of our investigational new drug, or IND, and/or clinical trial application, or CTA, submissions for our current and future product candidates;
- the ability of our Prime Editing technology to address unmet medical needs in patients;
- the implementation of our strategic plans for our business, programs and technology;
- the scope and duration of protection we are able to establish and maintain for intellectual property rights covering our Prime Editing technology;
- developments related to our competitors and our industry;
- our ability to leverage the clinical, regulatory, and manufacturing advancements made by gene therapy and gene editing programs to accelerate our clinical development and the regulatory approval of our product candidates;
- our ability to maintain existing collaborations or strategic relationships, to identify and enter into future license agreements and collaborations on favorable terms, if at all, and to realize the intended and potential benefits of such agreements and collaborations;
- developments related to our Prime Editing technology;
- regulatory developments in the United States and foreign countries;
- our ability to attract and retain key scientific and management personnel;
- the accuracy of our estimates regarding our expenses, capital requirements, and needs for additional financing;
- our anticipated use of net proceeds from this offering;
- our regulatory interactions with the U.S. Food and Drug Administration, or FDA, including with respect to the filing of a Biologics License Application for PM359 in the first half of 2027, based on the data from our Phase 1/2 trial of PM359 for the treatment of chronic granulomatous disease, or CGD, and the outcomes of any such interactions;

- the continued development and advancement of PM577a and PM647, including the timing of initial data for both in 2027;
- our ability to maintain an effective system of internal controls;
- the effect of unfavorable macroeconomic conditions or market volatility resulting from national or global economic conditions or geopolitical developments, including inflationary pressures and capital market disruptions, changes in or disruptions of U.S. governmental agencies, whether from a U.S. federal government shutdown or reduced resources, new or increased international tariffs and retaliatory tariffs, trade protection measures, military conflicts, economic sanctions and any economic slowdowns or recessions resulting from such developments, any of which could harm our research and development efforts, as well as the value of our securities and our ability to access capital markets; and
- our expectations regarding the anticipated timeline of our cash runway, future financial performance and our ability to continue as a going concern.

We caution you that the foregoing list of forward-looking statements made in this prospectus supplement, the accompanying prospectus and the documents we have filed with the SEC that are incorporated herein and therein by reference is not exclusive.

Any forward-looking statements in this prospectus supplement, the accompanying prospectus and the documents we have filed with the SEC that are incorporated herein and therein by reference reflect our current views with respect to future events or to our future financial performance and involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements.

We may from time-to-time provide estimates, projections and other information concerning our industry, our business and the markets for our programs and product candidates. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. Unless otherwise expressly stated, we obtained this industry, business, market, and other data from our own internal estimates and research as well as from reports, research surveys, studies, and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources. While we are not aware of any misstatements regarding any third-party information presented in this prospectus, their estimates, in particular, as they relate to projections, involve numerous assumptions, are subject to risks and uncertainties and are subject to change based on various factors.

Factors that may cause actual results to differ materially from current expectations include, among other things, those discussed in the “Risk Factors” section in this prospectus supplement, the section of the accompanying prospectus entitled “Risk Factors” and the risk factors and cautionary statements described in other documents that we file from time to time with the SEC, specifically under “Item 1A. Risk Factors” and elsewhere in our most recent Annual Report on Form 10-K for the year ended December 31, 2025, Quarterly Report on Form 10-Q for the quarter ended June 30, 2026, and any of our subsequent Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, as applicable. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights certain information about this offering and selected information contained elsewhere in or incorporated by reference into this prospectus supplement and the accompanying prospectus. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in shares of our common stock. For a more complete understanding of our Company and this offering, we encourage you to read and consider carefully the more detailed information in this prospectus supplement and the accompanying prospectus, including the information incorporated by reference into this prospectus supplement and the accompanying prospectus, and the information referred to under the heading "Risk Factors" in this prospectus supplement on page S-9 and on page 1 of the accompanying prospectus, and those identified in our most recent Annual Report on Form 10-K for the year ended December 31, 2025, Quarterly Report on Form 10-Q for the quarter ended June 30, 2026, any subsequent Quarterly Reports on Form 10-Q, and Current Reports on Form 8-K, as applicable.

Overview

We are a biotechnology company focused on developing a new class of genetic medicines designed to provide durable, and potentially curative, treatment options for patients with diseases driven by defined genetic alterations, acquired cellular dysfunction, or dysregulated gene expression. We believe Prime Editing has the potential to address approximately 90% of genetic diseases, as well as opportunities in non-genetic diseases.

We are advancing our *in vivo* programs to cure two of the largest genetic liver diseases, Wilson disease and alpha-1 antitrypsin deficiency, or AATD. In June 2026, we received clearance of the CTA for PM577a, an investigational Prime Editor for H1069Q-mutated Wilson disease, in New Zealand. In July 2026, the FDA cleared our IND application for PM577a in the United States. The H1069Q mutation is the most prevalent disease-causing mutation for Wilson disease in the United States and Europe. In October 2026, we announced that the first patient has been dosed in our global Phase 1/2 clinical trial of PM577a. We expect to report initial clinical data from the trial in 2027. Also in October 2026, we announced that the FDA has granted Rare Pediatric Disease designation to PM577. We intend to develop additional products to address additional pathogenic variants on a global basis. A follow-on candidate is in preclinical development targeting R778L, the most common mutant allele in East Asian populations.

In September 2026, the FDA cleared our IND application for PM647 in AATD, our investigational *in vivo* Prime Editor for AATD. This clearance enables PM647 to proceed to a global Phase 1/2 clinical study, initially in the United States, where approximately 100,000 people carry the PiZZ genotype. There are an estimated 200,000 people with AATD in the United States and European Union, of whom we estimate approximately 20,000 to 30,000 have been diagnosed. PM647 is designed to correct the E342K (Pi*Z) mutation in the SERPINA1 gene, the most common cause of AATD. We expect to report initial clinical data from the trial in 2027. We intend to leverage the modularity of our platform to expeditiously and efficiently develop these programs supported by our universal liver lipid nanoparticle along with potential regulatory, clinical and other synergies from our modular technology.

We also continue to advance our *in vivo* Cystic Fibrosis, or CF, program, which has been funded through multiple grants from the Cystic Fibrosis Foundation, and we plan to share proof-of-concept data for this program in 2026. We believe Prime Editing-based approaches could eventually benefit the vast majority of people with CF. We also continue our efforts to develop Prime Edited CAR-T products for hematology, immunology, and oncology in partnership with Bristol Myers Squibb, or BMS. In addition, we will continue to pursue additional business development opportunities to accelerate innovation, ensure the broadest application of Prime Editing, and further bolster our financial resources.

We continue to engage in regulatory dialogue with the FDA toward a Biologics License Application submission for PM359, which is planned for the first half of 2027. In June 2026, the FDA granted Regenerative Medicine Advanced Therapy, or RMAT, designation for PM359, which provides opportunities for intensive FDA guidance and potential expedited review during the program's development.

Recent Developments

Certain Unaudited Preliminary Financial Results

We estimate that our cash, cash equivalents, and short-term investments were approximately $61.2 million as of September 30, 2026, excluding our restricted cash of approximately $13.7 million. The foregoing information is based on preliminary unaudited information and management estimates as of and for the quarter ended September 30, 2026, is not a comprehensive statement of our financial results, and is subject to completion of our financial closing procedures. During our financial closing process our estimates can differ materially from our initial estimates presented herein based on our receipt of updated information. See the sections entitled "Risk Factors" and "Special Note Regarding Forward-Looking Statements" in this prospectus supplement and the documents incorporated by reference herein, for a discussion of certain factors that could result in differences between these preliminary unaudited estimates and the actual results. The preliminary financial data included in this prospectus supplement has been prepared by, and is the responsibility of, our management. PricewaterhouseCoopers LLP has not audited, reviewed, examined, compiled, nor applied agreed-upon procedures with respect to the preliminary financial data. Accordingly, PricewaterhouseCoopers LLP does not express an opinion or any other form of assurance with respect thereto.

These estimates should not be viewed as a substitute for interim financial statements prepared in accordance with accounting principles generally accepted in the United States and they are not necessarily indicative of the results to be achieved in any future period. Accordingly, you should not draw any conclusions based on the foregoing estimates and should not place undue reliance on these preliminary estimates. We assume no duty to update these preliminary estimates, except as required by law. Complete results as of September 30, 2026 will be included in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2026.

Corporate History and Information

We were incorporated under the laws of the State of Delaware in September 2019 under the name Prime Medicine, Inc. Our principal executive offices are located at 60 First Street, Cambridge, MA 02141, and our telephone number at that address is (617) 465-0013. We maintain an Internet website at the following address: *www.primemedicine.com*. The information contained in, or that can be accessed through, our website does not constitute a part of this prospectus supplement and is not incorporated by reference in this prospectus supplement or in any other filings we make with the SEC. We have included our website in this prospectus supplement solely as an inactive textual reference. Our common stock trades on The Nasdaq Global Market under the symbol "PRME."

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

We qualify as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, as amended (the "JOBS Act"). As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include:

- reduced disclosure about our executive compensation arrangements;
- not being required to hold advisory votes on executive compensation or to obtain stockholder approval of any golden parachute arrangements not previously approved; and
- an exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting.

We may take advantage of these exemptions until the fifth anniversary of our initial public offering or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company on the date that is the earliest of (i) the last day of the fiscal year in which we have total annual gross revenue of $1.235 billion or more; (ii) the last day of our fiscal year following the fifth anniversary of the date of the completion of our initial public offering; (iii) the date on which we have issued more than $1.07 billion in nonconvertible debt during the previous three years; or (iv) the last day of the fiscal year in which we are deemed to be a large accelerated filer under the rules of the SEC, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th. We may choose to take advantage of some but not all of these exemptions. We have taken advantage of reduced reporting requirements in this prospectus supplement. Accordingly, the information contained herein may be different from the information

you receive from other public companies in which you hold stock. Additionally, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to avail ourselves of this exemption and, therefore, while we are an emerging growth company, we will not be subject to new or revised accounting standards at the same time that they become applicable to other public companies that are not emerging growth companies. As a result of this election, our financial statements may not be comparable to those of other public companies that comply with new or revised accounting pronouncements as of public company effective dates.

We are also a “smaller reporting company” as defined in the Securities Exchange Act of 1934, as amended (the “Exchange Act”). We may continue to be a smaller reporting company even after we are no longer an emerging growth company. We may take advantage of certain of the scaled disclosures available to smaller reporting companies until the fiscal year following the determination that our stock held by non-affiliates is more than $250 million measured on the last business day of our second fiscal quarter, or our annual revenues are less than $100 million during the most recently completed fiscal year and our stock held by non-affiliates is more than $700 million measured on the last business day of our second fiscal quarter.

THE OFFERING

Common Stock We Are Offering Pursuant to this Prospectus Supplement	$125,000,000 of shares.
Option to Purchase Additional Shares	We have granted the underwriters an option for a period of 30 days from the date of this prospectus supplement to purchase up to $18,750,000 of additional shares of our common stock.
Common Stock to be Outstanding after this Offering	shares (or shares if the underwriters exercise their option to purchase additional shares in full).
Use of Proceeds	We estimate that the net proceeds to us from this offering will be approximately $ million, or approximately $ million if the underwriters exercise their option to purchase additional shares in full. We currently intend to use the net proceeds from this offering, together with our existing cash, cash equivalents, and short-term investments, to primarily support the advancement of our Wilson disease and AATD programs and other research and development activities, and the remainder for working capital, capital expenditures and other general corporate purposes. See "Use of Proceeds."
Risk Factors	Investing in our common stock involves significant risks. You should read the "Risk Factors" section of this prospectus supplement beginning on page S-9 and page 1 of the accompanying prospectus, and under similar headings in the other documents, including our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q, incorporated by reference into this prospectus supplement and the accompanying prospectus, for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.
Nasdaq Global Market Symbol	"PRME"

All information in this prospectus supplement related to the number of shares of our common stock to be outstanding immediately after this offering is based on 180,737,548 shares of our common stock outstanding as of June 30, 2026. The number of shares outstanding as of June 30, 2026 as used throughout this prospectus supplement, unless otherwise indicated, excludes:

- 22,547,914 shares of common stock issuable upon the exercise of time-based and vested performance-based stock options outstanding as of June 30, 2026, at a weighted average exercise price of $3.66 per share;
- 3,472,546 shares of common stock issuable upon the vesting of performance-based restricted common stock outstanding as of June 30, 2026;
- 10,808,408 shares of common stock available for future issuance under our 2022 Stock Option and Incentive Plan as of June 30, 2026, as well as any increases in the number of shares of common stock reserved for issuance thereunder; and
- 1,409,915 shares of common stock available for future issuance under our 2022 Employee Stock Purchase Plan as of June 30, 2026, as well as any increases in the number of shares of common stock reserved for issuance thereunder.

Unless otherwise stated, all information contained in this prospectus supplement assumes no exercise of stock options, no vesting of restricted common stock, no issuances of shares under the 2022 Employee Stock Purchase Plan after June 30, 2026, and no exercise by the underwriters of their option to purchase up to additional shares of our common stock in this offering.

In addition, the number of shares outstanding immediately after this offering does not include any shares of common stock sold after June 30, 2026, or that we may offer and sell in the future, pursuant to our Open Market Sale Agreement℠, dated November 3, 2023, or the Sales Agreement, with Jefferies LLC, as sales agent.

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before you decide to invest in our common stock, you should carefully consider the risks and uncertainties described below and in Part I, Item 1A. "Risk Factors" in our most recent Annual Report on Form 10-K for the year ended December 31, 2025, Quarterly Report on Form 10-Q for the quarter ended June 30, 2026, and any of our subsequent Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, as applicable, together with all other information contained in this prospectus supplement and in our filings with the SEC that we have incorporated by reference in this prospectus supplement. If any of the following risks actually occurs, our business, financial condition or results of operations could be adversely affected, which, in turn, could have a negative impact on the price of our common stock. In these circumstances, the market price of our common stock could decline, and you may lose all or part of your investment. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations. Please also read carefully the section above titled "Special Note Regarding Forward-Looking Statements."

Additional Risks Related to Our Common Stock and This Offering

Our preliminary financial results represent management's current estimates and are subject to change.

The preliminary financial results contained in "Prospectus Supplement Summary—Certain Unaudited Preliminary Financial Results" are only unaudited, preliminary estimates and are based on information available to management as of the date of this prospectus supplement and these estimates could change. Our actual financial results as of September 30, 2026 are subject to the completion of our condensed consolidated financial statements as of and for such period. Such actual financial results will not be available until after this offering is completed and, consequently, will not be available to you prior to investing in this offering. Our actual financial results as of September 30, 2026 may differ materially from the preliminary financial results we have provided as a result of the completion of our final adjustments, review by our independent registered public accounting firm and other developments arising between now and the time that our financial results for such period are finalized. Complete results as of September 30, 2026 will be included in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2026. See the other risks described in the sections entitled, "Prospectus Supplement Summary—Certain Unaudited Preliminary Financial Results" and "Special Note Regarding Forward-Looking Statements" for additional information regarding factors that could result in differences between these unaudited, preliminary financial results and the actual financial results we will report as of September 30, 2026.

If you purchase shares of our common stock in this offering, you will suffer immediate and substantial dilution.

If you purchase shares of our common stock in this offering, you will incur immediate and substantial dilution in the as adjusted net tangible book value of your stock because the price that you pay will be substantially greater than the net tangible book value per share of the shares you acquire. This dilution is due to our investors who purchased shares of our common stock prior to this offering having paid substantially less when they purchased their shares than the price at which shares of our common stock are being offered to the public in this offering. To the extent outstanding options are exercised, or outstanding restricted common stock vest, there will be further dilution to new investors. As a result of the dilution to your holdings, you may receive significantly less than the purchase price paid in this offering, if anything, in the event of a liquidation. For a further description of the dilution that you will experience immediately after this offering, see the section of this prospectus supplement titled "Dilution."

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

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 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 investors in this offering. The terms of these securities may

include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may be required to relinquish valuable rights to our technologies, intellectual property, potential future revenue streams, or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or other arrangements with third parties when needed, we may be required to delay, limit, reduce or terminate our product candidate development or future commercialization efforts or grant rights to third parties to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

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

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 business, financial condition or results of operations or enhance the value of our common stock. Furthermore, you will not have the opportunity as part of your investment decision to assess whether such proceeds are being used appropriately. Because of the number and variability of factors that will determine our use of our cash and cash equivalents, including the net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. Our management might not apply our cash and cash equivalents, including the net proceeds from this offering, in ways that ultimately increase the value of your investment. The net proceeds from this offering are intended to be used to primarily support the advancement of our Wilson disease and AATD programs and other research and development activities, and the remainder for working capital, capital expenditures and other general corporate purposes. Pending the use of net proceeds, we intend to invest the net proceeds in a variety of capital preservation instruments, including short-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the United States government.

The failure by our management to apply these funds effectively could result in financial losses that could harm our business, cause the price of our common stock to decline and delay the development of our current and future product candidates. Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

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

We have never declared or paid cash dividends on shares of our common stock. We anticipate that we will retain our earnings, if any, for future growth and therefore do not anticipate paying cash dividends in the future. As a result, only appreciation of the price of our shares of common stock will provide a return to shareholders.

Sales of a significant number of shares of our common stock in the public markets, or the perception that such sales could occur, could depress the market price of our common stock.

Sales of a substantial number of our shares in the public markets could occur at any time, and such sales, or the perception in the market that holders of a substantial number of our shares intend to sell their shares, could depress the market price of our common stock and impair our ability to raise capital through the sale of additional equity securities. We, our directors and our executive officers have agreed not to sell, dispose of or hedge any shares or securities convertible into or exchangeable for shares of common stock during the period from the date of this prospectus supplement continuing through and including the date 60 days after the date of this prospectus supplement, subject to certain exceptions. Jefferies LLC, TD Securities (USA) LLC, and Goldman Sachs & Co, LLC, as representatives of the underwriters, may, in their discretion, release the restrictions on any such shares at any time without notice. We cannot predict the effect that future sales of our common stock would have on the market price of our common stock.

USE OF PROCEEDS

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

We currently intend to use the net proceeds from this offering, together with our existing cash, cash equivalents, and short-term investments, to primarily support the advancement of our Wilson disease and AATD programs and other research and development activities, and the remainder for working capital, capital expenditures and other general corporate purposes. Pending the use of net proceeds, we intend to invest the net proceeds in a variety of capital preservation instruments, including short-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the United States government.

This expected use of our 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 expenditures may vary significantly depending on numerous factors, including the progress of our development, the status of and results from clinical trials, as well as any collaborations that we may enter into with third parties for our drug candidates, and any unforeseen cash needs, including the factors described under “Risk Factors” in this prospectus supplement and in the documents incorporated by reference herein. Due to the uncertainties inherent in the clinical development and regulatory approval process, it is difficult to estimate with certainty the exact amounts of the net proceeds from this offering that may be used for the above purposes. As such, our management will retain broad discretion over the use of the net proceeds from this offering and investors will be relying on the judgment of our management regarding the application of the proceeds from this offering.

DILUTION

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

As of June 30, 2026, we had net tangible book value of approximately $39.8 million, or $0.22 per share of our common stock, based upon 180,737,548 shares of our common stock outstanding as of that date. Historical net tangible book value per share is equal to our total tangible assets, less total liabilities, divided by the number of outstanding shares of our common stock. Dilution in net tangible book value per share represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the net tangible book value per share of our common stock immediately after this offering.

After giving further effect to our sale of shares of our common stock in this offering at the public offering price of $ per share, after deducting underwriting discounts and commissions and estimated offering expenses, our as-adjusted net tangible book value as of June 30, 2026 would have been $ million, or $ per share. This represents an immediate increase in net tangible book value of $ per share to existing stockholders and an immediate dilution in net tangible book value of $ per share to purchasers of common stock in this offering, as illustrated in the following table:

Public offering price per share		$
Historical net tangible book value per share as of June 30, 2026	$ 0.22	
Increase in net tangible book value per share attributable to this offering		
As-adjusted net tangible book value per share after this offering		
Dilution per share to purchasers of common stock in this offering		$

If the underwriters exercise their option to purchase up to additional shares in full at the public offering price of $ per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, the as-adjusted net tangible book value would be $ per share, representing an immediate increase in net tangible book value of $ per share to existing stockholders and an immediate dilution in as-adjusted net tangible book value of $ per share to new investors purchasing shares of our common stock in this offering.

The above discussion and table are based on 180,737,548 shares of our common stock outstanding as of June 30, 2026 and exclude:

- 22,547,914 shares of common stock issuable upon the exercise of time-based and vested performance-based stock options outstanding as of June 30, 2026, at a weighted average exercise price of $3.66 per share;
- 3,472,546 shares of common stock issuable upon the vesting of performance-based restricted common stock outstanding as of June 30, 2026;
- 10,808,408 shares of common stock available for future issuance under our 2022 Stock Option and Incentive Plan as of June 30, 2026, as well as any increases in the number of shares of common stock reserved for issuance thereunder; and
- 1,409,915 shares of common stock available for future issuance under our 2022 Employee Stock Purchase Plan as of June 30, 2026, as well as any increases in the number of shares of common stock reserved for issuance thereunder.

If the underwriters exercise in full their option to purchase up to additional shares, the number of shares of common stock held by existing stockholders will be reduced to % of the total number of shares of common stock to be outstanding after this offering.

To the extent that outstanding options are exercised, shares of common stock are issued upon the vesting of outstanding restricted common stock or under our 2022 Employee Stock Purchase Plan, new options are issued, or we otherwise issue additional shares of common stock in the future at a price less than the public offering price, you will experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities may result in further dilution to our stockholders.

DIVIDEND POLICY

We have never declared or paid cash dividends on our capital stock. We currently plan to retain all of our future earnings, if any, to finance the operation, development and growth of our business. Therefore, we do not expect to pay any cash dividends on our common stock in the foreseeable future. Payment of future dividends, if any, will be at the discretion of our board of directors and will depend on our financial condition, results of operations, capital requirements, restrictions contained in current or future financing instruments, provisions of applicable law and other factors the board deems relevant. Our ability to pay dividends on our common stock may be restricted by the terms of any of our future indebtedness.

UNDERWRITING

Subject to the terms and conditions set forth in the underwriting agreement, dated November , 2026, among us and Jefferies LLC, TD Securities (USA) LLC and Goldman Sachs & Co. LLC, as the representatives of the underwriters named below and the book-running managers of this offering, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us the respective number of shares of common stock shown opposite its name below:

Underwriter	Number of Shares
Jefferies LLC	
TD Securities (USA) LLC	
Goldman Sachs & Co, LLC	
Oppenheimer & Co, Inc.	
LifeSci Capital LLC	
Total	

The underwriting agreement provides that the obligations of the several underwriters are subject to certain conditions precedent such as the receipt by the underwriters of officers' certificates and legal opinions and approval of certain legal matters by their counsel. The underwriting agreement provides that the underwriters will purchase all of the shares of common stock if any of them are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

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

The underwriters have advised us that, following the completion of this offering, they currently intend to make a market in the common stock as permitted by applicable laws and regulations. However, the underwriters are not obligated to do so, and the underwriters may discontinue any market-making activities at any time without notice in their sole discretion. Accordingly, no assurance can be given as to the liquidity of the trading market for the common stock, that you will be able to sell any of the common stock held by you at a particular time or that the prices that you receive when you sell will be favorable.

The underwriters are offering the shares of common stock subject to their acceptance of the shares of common stock from us and subject to prior sale. The underwriters reserve the right to withdraw, cancel or modify offers and to reject orders in whole or in part.

Commission and Expenses

The underwriters have advised us that they propose to offer the shares of common stock to the public at the public offering price set forth on the cover page of this prospectus supplement and to certain dealers, which may include the underwriters, at that price less a concession not in excess of $ per share. After the offering, the public offering price, concession and reallowance to dealers may be reduced by the representatives. No such reduction will change the amount of proceeds to be received by us as set forth on the cover page of this prospectus supplement.

The following table shows the public offering price, the underwriting discounts and commissions that we are to pay the underwriters and the proceeds, before expenses, to us in connection with this offering. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	Per Share		Total	
	Without Option	With Option	Without Option	With Option
Public offering price				
Underwriting discounts and commissions				
Proceeds, before expenses, to Prime Medicine, Inc.				

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately $. We have also agreed to reimburse the underwriters for certain of their expenses in an amount up to $40,000.

Listing

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

Option to Purchase Additional Shares

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus supplement, to purchase, from time to time, in whole or in part, up to an aggregate of shares from us at the public offering price set forth on the cover page of this prospectus supplement, less underwriting discounts and commissions. If the underwriters exercise this option, each underwriter will be obligated, subject to specified conditions, to purchase a number of additional shares proportionate to that underwriter's initial purchase commitment as indicated in the table above.

No Sales of Similar Securities

We, our officers and directors have agreed, subject to specified exceptions, not to:

- offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend, or otherwise transfer or dispose of, directly or indirectly; or
- enter into any hedging, swap or other agreement or transaction that transfers, in whole or in part, any of the economic consequences of; or
- make any demand for or exercise any right with respect to the registration of, any common stock or securities convertible into or exchangeable or exercisable for any common stock.

This restriction terminates after the close of trading of the common stock on and including the 60th day after the date of this prospectus supplement; *provided*, that with respect to sales pursuant to the Sales Agreement, this restriction terminates upon the earlier of (x) the exercise in full by the underwriters of their option to purchase additional shares of common stock pursuant to the underwriting agreement and (y) the 30th day after the date of this prospectus supplement.

With respect to our directors and officers, subject to certain conditions, this restriction does not apply to transfer of shares of common stock: (i) as a *bona fide* gift or gifts, or for bona fide estate planning purposes, (ii) by will or intestacy or other testamentary document, (iii) to any trust for the direct or indirect benefit of the lock-up party or the immediate family of the lock-up party, or if the lock-up party is a trust, to a trust or beneficiary of the trust or to the estate of a beneficiary of such trust, (iv) to a corporation, partnership, limited liability company, investment fund or other entity (A) of which the lock-up party and/or the immediate family of the lock-up party are, directly or indirectly, the legal and beneficial owner of all of the outstanding equity securities or similar interests, or (B) controlled by, or under common control with, the lock-up party or the immediate family of the lock-up party, (v) to a nominee or custodian of a person or entity to whom a disposition or transfer would be permissible under clauses (i) through (iv) above, (vi) if the lock-up party is a corporation, partnership, limited liability company, trust or other business entity, (A) to another corporation, partnership, limited liability company, trust, or other business entity that is an affiliate (as defined in Rule 405 promulgated under the Securities Act) of the lock-up party, or to any investment fund or other entity controlling, controlled by, managing or managed by or under common control or common investment management with the lock-up party or affiliates of the lock-up party (including where the lock-up party is a partnership, to its general partner or a

successor partnership or fund, or any other funds managed by such partnership), or (B) as part of a distribution, transfer or disposition to limited partners, members or shareholders of the lock-up party, (vii) by operation of law, such as pursuant to a qualified domestic order, divorce settlement, divorce decree or separation agreement, (viii) to us from an employee upon death, disability or termination of employment, in each case, of such employee, (ix) as part of a sale or other transaction involving the lock-up party's or its direct or indirect affiliates' lock-up securities acquired in this offering, subject to certain exceptions, or in open market transactions after the pricing date for this offering, (x) to us in connection with the vesting, settlement, or exercise of restricted stock units, options, warrants or other rights to purchase shares of common stock (including, in each case, by way of "net" or "cashless" exercise), (xi) pursuant to a bona fide third-party tender offer, merger, consolidation or other similar transaction that is approved by our board of directors and made to all holders of our capital stock involving a "change of control", or (xii) pursuant to any trading plan pursuant to Rule 10b5-1 under the Exchange Act that was entered into by the lock-up party prior to the date of the lock-up agreement; provided that (A) in the case of any transfer or distribution pursuant to clause (i), (ii), (iii), (iv), (v) and (vii), such transfer shall not involve a disposition for value and each donee, devisee, transferee or distributee shall execute and deliver to the representatives a lock-up letter in the form of the lock-up agreement, (B) in the case of any transfer or distribution pursuant to clause (i), (ii), (iii), (iv), (v), (vi) and (ix) no filing by any party under the Exchange Act or other public announcement shall be required or shall be made voluntarily in connection with such transfer or distribution, (C) in the case of any transfer or distribution pursuant to clause (vii), (viii) and (x) it shall be a condition to such transfer that no public filing, report or announcement shall be voluntarily made and if any filing under Section 16(a) of the Exchange Act, or other public filing, report or announcement reporting a reduction in beneficial ownership of shares of common stock shall be legally required during the restricted period, such filing, report or announcement shall clearly indicate in the footnotes thereto the nature and conditions of such transfer, and (D) in the case of any transfer or distribution pursuant to clause (xii), any filing required to be made under Section 16(a) of the Exchange Act shall state that such transfer or distribution is pursuant to such 10b5-1 plan. Furthermore, the lock-up parties may (a) exercise outstanding options, settle restricted stock units or other equity awards or exercise warrants pursuant to plans described in this prospectus; (b) convert outstanding preferred stock, warrants to acquire preferred stock or convertible securities into shares of common stock or warrants to acquire shares of common stock; and (c) establish 10b5-1 plans, provided that (1) such plans do not provide for the transfer of lock-up securities during the restricted period and (2) such filing or announcement shall include a statement to the effect that no transfers may be made pursuant to such 10b5-1 plan during the restricted period.

In addition, the foregoing restrictions shall not apply to the establishment of a plan that satisfies all of the requirements of Rule 10b5-1(c)(1)(i)(B) under the Exchange Act; provided that no sales of the security holder's shares of common stock shall be made pursuant to such a plan prior to the expiration of the lock-up period.

Jefferies LLC, TD Securities (USA) LLC and Goldman Sachs & Co. LLC, in their sole discretion and at any time or from time to time before the termination of the 60-day period, may release all or any portion of the shares of common stock subject to lock-up agreements. There are no existing agreements between the underwriters and any of our shareholders who will execute a lock-up agreement, providing consent to the sale of shares prior to the expiration of the lock-up period.

Stabilization

The underwriters have advised us that, pursuant to Regulation M under the Exchange Act, certain persons participating in the offering may engage in short sale transactions, stabilizing transactions, syndicate covering transactions or the imposition of penalty bids in connection with this offering. These activities may have the effect of stabilizing or maintaining the market price of the common stock at a level above that which might otherwise prevail in the open market. Establishing short sales positions may involve either "covered" short sales or "naked" short sales.

"Covered" short sales are sales made in an amount not greater than the underwriters' option to purchase additional shares of our common stock in this offering. The underwriters may close out any covered short position by either exercising their option to purchase additional shares of our common stock or purchasing shares of our common stock in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in

the open market as compared to the price at which they may purchase shares through the option to purchase additional shares.

“Naked” short sales are sales in excess of the option to purchase additional shares of our common stock. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares of common stock in the open market after pricing that could adversely affect investors who purchase in this offering.

A stabilizing bid is a bid for the purchase of shares of common stock on behalf of the underwriters for the purpose of fixing or maintaining the price of the common stock. A syndicate covering transaction is the bid for or the purchase of shares of common stock on behalf of the underwriters to reduce a short position incurred by the underwriters in connection with the offering. Similar to other purchase transactions, the underwriters’ purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. A penalty bid is an arrangement permitting the underwriters to reclaim the selling concession otherwise accruing to a syndicate member in connection with the offering if the common stock originally sold by such syndicate member is purchased in a syndicate covering transaction and therefore has not been effectively placed by such syndicate member.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. The underwriters are not obligated to engage in these activities and, if commenced, any of the activities may be discontinued at any time.

The underwriters may also engage in passive market making transactions in our common stock on The Nasdaq Global Market in accordance with Rule 103 of Regulation M during a period before the commencement of offers or sales of shares of our common stock in this offering and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker’s bid, that bid must then be lowered when specified purchase limits are exceeded.

Electronic Distribution

A prospectus supplement in electronic format may be made available by e-mail or on the web sites or through online services maintained by one or more of the underwriters or their affiliates. In those cases, prospective investors may view offering terms online and may be allowed to place orders online. The underwriters may agree with us to allocate a specific number of shares of common stock for sale to online brokerage account holders. Any such allocation for online distributions will be made by the underwriters on the same basis as other allocations. Other than the prospectus supplement in electronic format, the information on the underwriters’ web sites and any information contained in any other web site maintained by any of the underwriters is not part of this prospectus supplement, has not been approved and/or endorsed by us or the underwriters and should not be relied upon by investors.

Other Activities and Relationships

The underwriters and certain of their affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriters and certain of their affiliates have, from time to time, performed, and may in the future perform, various commercial and investment banking and financial advisory services for us and our affiliates, for which they received or will receive customary fees and expenses. For example, Jefferies LLC is our sales agent pursuant to the Sales Agreement, pursuant to which we may offer and sell, from time to time, shares of our common stock through an “at the market offering” as defined in Rule 415(a)(4) promulgated under the Securities Act.

In the ordinary course of their various business activities, the underwriters and certain of their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers, and such investment and securities activities may involve securities and/or instruments issued by us and our affiliates. If the underwriters or their respective affiliates have a lending relationship with us, they routinely hedge their credit exposure to us consistent with their customary risk management policies. The underwriters and their respective affiliates may hedge such exposure by entering into transactions which consist of either the purchase of credit default swaps or the creation of short positions in our securities or the securities of our affiliates, including potentially the common stock offered hereby. Any such short positions could adversely affect future trading prices of the common stock offered hereby. The underwriters and certain of their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Disclaimers About Non-U.S. Jurisdictions

Notice to Prospective Investors in the European Economic Area

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

a. to any legal entity which is a "qualified investor" as defined under Article 2 of the Prospectus Regulation;
b. to fewer than 150 natural or legal persons (other than qualified investors as defined under Article 2 of the Prospectus Regulation), subject to obtaining the prior consent of representatives for any such offer; or
c. in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of securities shall require us or any of the representatives 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 "offer to the public" in relation to the securities in any Relevant State means the communication in any form and by any means of sufficient information on the terms of the offer and any 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

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 shares which has been approved by the Financial Conduct Authority, except that the shares may be offered to the public in the United Kingdom at any time:

a. to any legal entity which is a qualified investor as defined under Article 2 of the UK Prospectus Regulation;
b. 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
c. in any other circumstances falling within Section 86 of the FSMA,

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

For the purposes of this provision, the expression an "offer to the public" in relation to the shares 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 shares to be offered so as to enable an investor to decide to purchase or subscribe for any shares 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.

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 shares of common stock 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

(A) Resale Restrictions

The distribution of 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.

(B) Representations of Canadian Purchasers

By purchasing 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 or Section 73.3(1) of the Securities Act (Ontario), as applicable,
- the purchaser is a “permitted client” as defined in 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.

(C) Conflicts of Interest

Canadian purchasers are hereby notified that certain of the underwriters are relying on the exemption set out in section 3A.3 or 3A.4, if applicable, of National Instrument 33-105 - *Underwriting Conflicts* from having to provide certain conflict of interest disclosure in this document.

(D) 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.

(E) 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.

(F) Taxation and Eligibility for Investment

Canadian purchasers of 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.

(G) Language of Documents

The purchaser confirms its express wish and that it has requested that this document, all documents evidencing or relating to the sale of the securities described herein and all other related documents be drawn up exclusively in the English language. *L'acquéreur confirme sa volonté expresse et qu'il a demandé que le présent document, tous les documents attestant de la vente des titres décrits dans le présent document ou s'y rapportant ainsi que tous les autres documents s'y rattachant soient rédigés exclusivement en langue anglaise.*

Notice to Prospective Investors in Australia

This prospectus supplement and the accompanying prospectus are not a disclosure document for the purposes of Australia's Corporations Act 2001 (Cth) of Australia, or Corporations Act, have not been lodged with the Australian Securities & Investments Commission and are only directed to the categories of exempt persons set out below. Accordingly, if you receive this prospectus supplement and the accompanying prospectus in Australia:

a. 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 which 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" within the meaning of 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.

b. 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 are being distributed only to, and are 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 have 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, the accompanying prospectus, nor any other offering or marketing material relating to the offering, the Company or the securities 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 ("CISA"). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of securities.

LEGAL MATTERS

The validity of the shares of common stock offered by this prospectus supplement and the accompanying prospectus will be passed upon by Goodwin Procter LLP, Boston, Massachusetts. Paul Hastings LLP, New York, New York, has acted as counsel for the underwriters in connection with this offering.

EXPERTS

The financial statements incorporated in this prospectus supplement by reference to the Annual Report on Form 10-K for the year ended December 31, 2025 have been so incorporated in reliance on the report (which contains an explanatory paragraph relating to the Company's ability to continue as a going concern as described in Note 1 to the financial statements) of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

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 *www.sec.gov* and on our investor website at *www.primemedicine.com*. Information contained in or accessible through our website is not a part of this prospectus supplement or the accompanying prospectus and is not incorporated by reference in this prospectus supplement or the accompanying prospectus.

This prospectus supplement and the accompanying prospectus is part of a registration statement on Form S-3 that we filed with the SEC and does not contain all of the information in the registration statement. The full registration statement may be obtained from the SEC or us, as provided above. Statements in this prospectus supplement and the accompanying prospectus about any documents filed as exhibits to the registration statement are summaries, and each statement is qualified in all respects by reference to the document to which it refers. You should refer to the actual documents for a more complete description of the relevant matters. You may inspect a copy of the registration statement through the SEC's website, as provided above.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference in this prospectus supplement and the accompanying prospectus much of the information we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information incorporated by reference is considered to be part of this prospectus supplement and the accompanying prospectus, and later information that we file with the SEC (Commission File No. 001-41536) will automatically update and supersede this information. We incorporate by reference the documents listed below and any future filings made by us with the SEC (other than Current Reports on Form 8-K or portions thereof furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items and other portions of documents that are furnished, but not filed, pursuant to applicable rules promulgated by the SEC) that are filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus supplement and prior to the termination of offerings of securities covered by this prospectus supplement:

- Annual Report on Form 10-K for the fiscal year ended December 31, 2025, filed with the SEC on March 3, 2026;
- The information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2025 from our definitive proxy statement on Schedule 14A (other than information furnished rather than filed), which was filed with the SEC on April 23, 2026;
- Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2026 and June 30, 2026, filed with the SEC on May 7, 2026 and on August 6, 2026, respectively;
- Current Reports on Form 8-K (other than information furnished rather than filed) filed with the SEC on April 16, 2026, June 8, 2026, July 8, 2026, and November 10, 2026; and
- The description of our common stock contained in our Registration Statement on Form 8-A (File No. 001-41536) as filed with the SEC on October 17, 2022, including any amendments or reports filed for the purpose of updating such description, including Exhibit 4.3 to our Annual Report on Form 10-K for the year ended December 31, 2025, as filed with the SEC on March 3, 2026.

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

Prime Medicine, Inc.
60 First Street
Cambridge, MA 02141
(617) 465-0013

You may also access these documents, free of charge on the SEC's website at *www.sec.gov* or on our website at *www.primemedicine.com*. Information contained in or accessible through our website does not constitute a part of this prospectus supplement and is not incorporated by reference in this prospectus supplement. We have included our website solely as an inactive textual reference.

This prospectus supplement and the accompanying prospectus are part of a registration statement we filed with the SEC. We have incorporated exhibits into the registration statement. You should read the exhibits carefully for provisions that may be important to you.

You should rely only on the information incorporated by reference or provided in this prospectus supplement and the accompanying prospectus. We have not authorized anyone to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus supplement, the accompanying prospectus or in the documents incorporated by reference is accurate as of any date other than the date on the front of this prospectus supplement or those documents.

In accordance with Rule 412 of the Securities Act, any statement contained in a document incorporated by reference herein shall be deemed modified or superseded to the extent that a statement contained herein or in any other subsequently filed document which also is or is deemed to be incorporated by reference herein modifies or supersedes such statement.

PROSPECTUS



$500,000,000

Common Stock
Preferred Stock
Debt Securities
Warrants
Units

We may from time to time issue, in one or more series or classes, offer and sell up to $500,000,000 in aggregate principal amount of our common stock, preferred stock, debt securities, warrants and/or units, in any combination, together or separately, in one or more offerings in amounts, at prices and on the terms that we will determine at the time of the offering and which will be set forth in a prospectus supplement to this prospectus and any related free writing prospectus.

Each time we sell securities described herein, we will provide prospective investors with a supplement to this prospectus that will specify the terms of the securities being offered. We may sell these securities to or through underwriters or dealers and also to other purchasers or through agents. We will set forth the names of any underwriters or agents, and any fees, conversions, or discount arrangements, in the applicable prospectus supplement. For additional information on the methods of sale, you should refer to the section entitled "Plan of Distribution" in this prospectus and in the applicable prospectus supplement. We may not sell any securities under this prospectus without delivery of the applicable prospectus supplement. You should read this document and any prospectus supplement or amendment carefully before you invest in our securities.

We are an "emerging growth company" and "smaller reporting company" under the federal securities laws and, as such, are subject to reduced public company reporting requirements. See "Prospectus Summary—Implications of Being an Emerging Growth Company and Smaller Reporting Company."

Our common stock is listed on The Nasdaq Global Market under the symbol "PRME." On February 25, 2026, the closing price for our common stock, as reported on The Nasdaq Global Market, was $4.13 per share. The applicable prospectus supplement will contain information, where applicable, as to any other listing on The Nasdaq Global Market or any securities market or other exchange of the securities, if any, covered by the prospectus supplement.

Investing in these securities involves certain risks. See "Risk Factors" on page 1 of this prospectus as well as those 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.

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 March 3, 2026.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission (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 $500,000,000.

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities described herein, we will provide one or more prospectus supplements that will contain specific information about the terms of the offering. The prospectus supplement may also add, update or change information contained in this prospectus. This prospectus, together with any accompanying prospectus supplement, contains important information you should know before investing in our securities, including important information about us and the securities being offered. You should read both this prospectus, any applicable accompanying prospectus supplement, and any related free writing prospectus, together with the additional information described under the headings "Where You Can Find More Information" and "Incorporation of Certain Information by Reference" beginning on page 33 of this prospectus.

You should rely only on the information contained in or incorporated by reference in this prospectus, any accompanying prospectus supplement or in any related free writing prospectus filed by us with the SEC. We have not authorized anyone to provide you with different information. This prospectus does not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in any 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 accompanying 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. This prospectus, any applicable prospectus supplement and the information incorporated herein or therein by reference contains market data, industry statistics and other data that have been obtained or compiled from information made available by independent third parties. We are responsible for all of the disclosures contained in this prospectus, and we believe that these sources are reliable; however, we have not independently verified the information contained in such publications.

THIS PROSPECTUS MAY NOT BE USED TO OFFER AND SELL SECURITIES UNLESS IT IS ACCOMPANIED BY AN ADDITIONAL PROSPECTUS OR A PROSPECTUS SUPPLEMENT.

As used in this prospectus, unless the context otherwise requires, references to the terms "Prime," "Prime Medicine," "the Company," "we," "us" and "our," and similar designations refer to Prime Medicine, Inc. and, where appropriate, our wholly-owned subsidiary.

We intend to apply for various trademarks that we use in connection with the operation of our business. This prospectus may also contain trademarks, service marks and trade names of third parties, which are the property of their respective owners. Our use or display of third parties' trademarks, service marks, trade names or products in this prospectus is not intended to, and does not imply a relationship with, or endorsement or sponsorship by us. Solely for convenience, the trademarks, service marks and trade names referred to in this prospectus may appear without the ®, SM and ™ symbols, but the omission of such references is not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the right of the applicable owner of these trademarks, service marks and trade names.

RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully consider the risks set forth in our filings with the SEC that are incorporated by reference herein and any prospectus supplement, as well as other information we include or incorporate by reference into this prospectus and any applicable prospectus supplement, before making an investment decision. Our business, financial condition or results of operations could be materially adversely affected by the materialization of any of these risks. The trading price of our securities could decline due to the materialization of any of these risks, and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently believe to be immaterial may also adversely affect our business.

This prospectus and the documents incorporated herein by reference also contain forward-looking statements that involve risks and uncertainties. Actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks described in the documents incorporated herein by reference, including our Annual Report on Form 10-K for the fiscal year ended December 31, 2025 and the other documents we file with the SEC that are deemed incorporated by reference into this prospectus. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also adversely affect our operations. See the sections titled "Where You Can Find More Information" and "Incorporation of Certain Information by Reference."

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the documents that we incorporate by reference, includes forward-looking statements within the meaning of Section 27A of the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). All statements, other than statements of historical fact, contained herein, including statements regarding our plans, objectives and expectations for our business, operations and financial performance and condition, and can be identified by terminology such as "anticipate," "believe," "contemplate," "continue" "could," "estimate," "estimate," "expect," "goal," "hope," "intend," "may," "might," "plan," "possible," "potential," "predict," "project," "seek," "should," "strategy," "target," "will," "would," "can," "future" or the negative of these words or other similar expressions. Forward-looking statements are based on management's belief and assumptions and on information currently available to management. Although we believe that the expectations reflected in forward-looking statements are reasonable, such statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by forward-looking statements.

These forward-looking statements include, but are not limited to, statements about:

- the initiation, timing, progress and results of our research and development programs, product candidates, and ongoing and future preclinical studies and future clinical trials;
- our ability to demonstrate, and the timing of, preclinical proof-of-concept in vivo for multiple programs;
- our ability to advance any current and future product candidates that we may identify and successfully complete any clinical trials, including the manufacture of any such product candidates;
- our ability to pursue our areas of focus and any other additional programs we may advance;
- our ability to quickly leverage programs within our initial target indications and to progress additional programs to further develop our pipeline;
- the timing of our investigational new drug ("IND") application submissions;
- the ability of our Prime Editing technology to address unmet medical needs in patients;
- the implementation of our strategic plans for our business, programs and technology;
- the scope and duration of protection we are able to establish and maintain for intellectual property rights covering our Prime Editing technology;
- developments related to our competitors and our industry;
- our ability to leverage the clinical, regulatory, and manufacturing advancements made by gene therapy and gene editing programs to accelerate our clinical trials and approval of product candidates;
- our ability to maintain existing collaborations or strategic relationships, to identify and enter into future license agreements and collaborations on favorable terms, if at all, and to realize the intended and potential benefits of such agreements and collaborations;
- developments related to our Prime Editing technology;
- regulatory developments in the United States and foreign countries;
- our ability to attract and retain key scientific and management personnel;
- the accuracy of our estimates regarding our expenses, capital requirements and needs for additional financing;
- our planned regulatory interactions with the U.S. Food and Drug Administration based on the data from our

Phase 1/2 trial of PM359 for the treatment of chronic granulomatous disease ("CGD"), and the outcomes of any such interactions;

- our ability to maintain an effective system of internal controls;
- the effect of unfavorable macroeconomic conditions or market volatility resulting from national or global economic conditions or geopolitical developments, including high inflation and capital market disruptions, changes in or disruptions of U.S. governmental agencies, whether from a U.S. federal government shutdown or reduced resources, new or increased international tariffs and retaliatory tariffs, trade protection measures, economic sanctions and economic slowdowns or recessions that may result from such developments which could harm our research and development efforts as well as the value of our securities and our ability to access capital markets;
- our expectations regarding the anticipated timeline of our cash runway, future financial performance, and our ability to continue as a going concern;
- our anticipated use of net proceeds from any offering of our securities pursuant to this prospectus; and
- other risks and uncertainties, including those listed under the caption "Risk Factors" and elsewhere in our Annual Report on Form 10-K for the fiscal year ended December 31, 2025 and the section of any accompanying prospectus supplement entitled "Risk Factors," as well as in other filings make with the SEC subsequent to the date hereof that are incorporated by reference herein.

The forward-looking statements in this prospectus represent our views as of the date of this prospectus. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should therefore not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this prospectus.

We may from time to time provide estimates, projections and other information concerning our industry, our business and the markets for our programs and product candidates. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. Unless otherwise expressly stated, we obtained this industry, business, market, and other data from our own internal estimates and research as well as from reports, research surveys, studies, and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources. While we are not aware of any misstatements regarding any third-party information presented in this prospectus, their estimates, in particular, as they relate to projections, involve numerous assumptions, are subject to risks and uncertainties and are subject to change based on various factors.

You should read this prospectus, any applicable prospectus supplement and any related free writing prospectus and the documents that we reference therein and have filed with the SEC as exhibits thereto completely and with the understanding that our actual future results may be materially different from any future results expressed or implied by these forward-looking statements. These estimates involve numerous assumptions, are subject to risks and uncertainties and are subject to change based on various factors, including those discussed under Part I, Item 1A. "Risk Factors" and elsewhere in our Annual Report on Form 10-K for the fiscal year ended December 31, 2025 and the section of any accompanying prospectus supplement entitled "Risk Factors", as well as in other filings make with the SEC subsequent to the date hereof that are incorporated by reference herein. If one or more of these risks or uncertainties occur, or if our underlying assumptions prove to be incorrect, actual events or results may vary significantly from those implied or projected by the forward-looking statements. No forward-looking statement is a guarantee of future performance.

OUR COMPANY

Overview

We are a biotechnology company focused on developing a new class of genetic medicines designed to provide durable, and potentially curative, treatment options for patients with diseases driven by defined genetic alterations, acquired cellular dysfunction, or dysregulated gene expression. Our approach is grounded in Prime Editing, a next-generation gene editing technology that enables targeted modifications to genomic DNA without introducing double-stranded breaks. We believe Prime Editing represents the most versatile and precise method for rewriting, replacing, or repairing DNA sequences and may allow us to address a broad spectrum of diseases with an improved safety and specificity profile relative to earlier editing technologies. We are advancing a pipeline of wholly owned in vivo programs targeting diseases of the liver, Cystic Fibrosis ("CF") programs with the support of the Cystic Fibrosis Foundation and partnered ex vivo programs with Bristol Myers Squibb ("BMS"), supported by our modular delivery and Prime Editor platform. Early clinical data from our ex vivo program, PM359 for CGD, have demonstrated restoration of functional protein activity in treated patients, providing clinical validation of Prime Editing and a potentially curative treatment for CGD patients.

Genetic diseases affecting the liver and lung, as well as hematologic disorders addressed through ex vivo editing, represent our initial development priorities. Many of these diseases arise from well-characterized mutations, have established natural histories, and impose meaningful clinical burdens on patients, caregivers and physicians despite available standard-of-care therapies. We believe these attributes enable efficient clinical development, clear biomarker-driven readouts, and the potential to demonstrate meaningful patient benefit in early-stage clinical studies. Our lead program, PM577 for Wilson Disease, is designed to initially correct the H1069Q mutation in the ATP7B gene and is supported by preclinical data showing targeted correction and restoration of copper homeostasis in animal models. We are also developing follow-on Prime Editors capable of addressing additional ATP7B mutations, enabling a modular and efficient expansion of the Wilson franchise. In addition, PM647 is being advanced for alpha-1 antitrypsin deficiency, another liver targeted disease with substantial unmet need. Beyond these efforts, we are progressing a program in CF using Prime Editing delivered via lipid nanoparticles or adeno-associated viruses.

We have constructed an integrated Prime Editing platform engineered to support rapid iteration, standardized manufacturing, and shared toxicology and Chemistry, Manufacturing, and Controls, pathways across programs, thereby enabling efficient advancement of multiple therapeutic candidates. By maintaining core delivery and editor components while altering program-specific guide RNAs and repair templates, we believe we can leverage platform-level knowledge to expedite new candidate identification and streamline IND-enabling activities, especially within common tissues.

Our organization is intentionally structured to support clinical development and regulatory engagement as we prepare for multiple parallel clinical trials. We are investing in scalable manufacturing and quality systems capable of supporting clinical supply for our lead programs. Consistent with industry practice, we also seek to augment our internal capabilities through collaborations. Our partnership with BMS, focused on applying Prime Editing to ex vivo T-cell engineering, reflects the potential applicability of Prime Editing across therapeutic modalities. We believe the insights gained through this collaboration may inform future applications of Prime Editing in immunology and oncology.

Looking ahead, our strategy is to advance Prime Editing programs through clinical development, leverage our modular platform to expand into additional indications, and pursue disciplined portfolio prioritization anchored in clear scientific, development, and commercial criteria. We expect our focus on liver-directed in vivo editing, combined with the modularity of our platform, will allow us to build a pipeline with breadth and depth while maintaining operational efficiency and disciplined capital deployment. Ultimately, our goal is to translate Prime Editing into a clinically and commercially validated therapeutic modality for the treatment across an array of severe genetic diseases and tissue types.

Corporate History

We were incorporated under the laws of the State of Delaware in September 2019 under the name Prime Medicine,

Inc. Our principal executive offices are located at 60 First Street, Cambridge, MA 02141 and our telephone number at that address is (617) 465-0013. Our website address is www.primemedicine.com. The information contained in, or that can be accessed through, our website, does not constitute a part of this prospectus, and is not incorporated by reference in this prospectus or in any other filings we make with the SEC. We have included our website in this prospectus solely as an inactive textual reference. Our common stock trades on The Nasdaq Global Market under the symbol "PRME."

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

We qualify as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, as amended (the "JOBS Act"). As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include:

- reduced disclosure about our executive compensation arrangements;
- not being required to hold advisory votes on executive compensation or to obtain stockholder approval of any golden parachute arrangements not previously approved;
- an exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting pursuant to the Sarbanes-Oxley Act of 2002; and
- an exemption from compliance with the requirements of the Public Company Accounting Oversight Board regarding the communication of critical audit matters in the auditor's report on the financial statements.

We may take advantage of these exemptions until the fifth anniversary of our initial public offering or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company on the date that is the earliest of (i) the last day of the fiscal year in which we have total annual gross revenue of $1.235 billion or more; (ii) the last day of our fiscal year following the fifth anniversary of the date of the completion of our initial public offering; (iii) the date on which we have issued more than $1.0 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the SEC, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th. We may choose to take advantage of some but not all of these exemptions. We have taken advantage of reduced reporting requirements in this prospectus. Accordingly, the information contained herein may be different from the information you receive from other public companies in which you hold stock. Additionally, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to avail ourselves of this exemption and, therefore, while we are an emerging growth company, we will not be subject to new or revised accounting standards at the same time that they become applicable to other public companies that are not emerging growth companies. As a result of this election, our financial statements may not be comparable to those of other public companies that comply with new or revised accounting pronouncements as of public company effective dates. We may choose to early adopt any new or revised accounting standards whenever such early adoption is permitted for private companies.

We are also a "smaller reporting company," as defined in Rule 12b-2 under the Exchange Act. We may continue to be a smaller reporting company even after we are no longer an emerging growth company. We may take advantage of certain of the scaled disclosures available to smaller reporting companies until the fiscal year following the determination that our stock held by non-affiliates is more than $250 million measured on the last business day of our second fiscal quarter, or our annual revenues are more than $100 million during the most recently completed fiscal year and our stock held by non-affiliates is more than $700 million measured on the last business day of our second fiscal quarter.

USE OF PROCEEDS

We will retain broad discretion over the use of the net proceeds from the sale of the securities offered hereby. Except as described in any applicable prospectus supplement or in any free writing prospectus that we may authorize to be provided to you in connection with a specific offering, we currently intend to use the net proceeds from the sale of the securities offered hereby for general corporate purposes. General corporate purposes may include, without limitation, research and development and clinical development costs to support the advancement of our product candidates and the expansion of our research and development programs; working capital; capital expenditures; and other general corporate purposes. We may temporarily invest the net proceeds in a variety of capital preservation instruments, including short-term, investment-grade, interest-bearing instruments and U.S. government securities, or may hold such proceeds as cash, until they are used for their stated purpose. We have not determined the amount of net proceeds to be used specifically for such purposes. As a result, management will retain broad discretion over the allocation of net proceeds.

SECURITIES THAT MAY BE OFFERED

This prospectus contains summary descriptions of the securities we may offer from time to time. These summary descriptions are not meant to be complete descriptions of each security. The particular terms of any security will be described in the applicable prospectus supplement. This prospectus provides you with a general description of the securities we may offer. Each time we sell securities described herein, we will provide prospective investors with a supplement to this prospectus that will contain specific information about the terms of that offering, including the specific amounts, prices and terms of the securities offered.

We may sell the securities to or through underwriters, dealers or agents, directly to purchasers or through a combination of any of these methods of sale or as otherwise set forth below under “Plan of Distribution.” We, as well as any agents acting on our behalf, reserve the sole right to accept and to reject in whole or in part any proposed purchase of securities. Any prospectus supplement will set forth the names of any underwriters, dealers, agents or other entities involved in the sale of securities described in that prospectus supplement and any applicable fee, commission or discount arrangements with them.

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock is intended as a summary only and therefore is not a complete description of our capital stock. This description is based upon, and is qualified in its entirety by reference to, our third amended and restated certificate of incorporation, as amended (our "certificate of incorporation"), our second amended and restated bylaws (our "bylaws"), and applicable provisions of Delaware corporate law. You should read our certificate of incorporation and our bylaws, in each case, as amended and supplemented, which are filed as exhibits to the registration statement of which this prospectus forms a part, for the provisions that are important to you.

General

Our authorized capital stock consists of 775,000,000 shares of common stock, par value $0.00001 per share and 10,000,000 shares of preferred stock, par value $0.00001 per share, all of which shares of preferred stock are undesignated. The following description of our capital stock and provisions of our certificate of incorporation and bylaws are summaries and are qualified by reference to our certificate of incorporation and our bylaws, in each case, as amended and supplemented.

Common Stock

As of December 31, 2025, we had outstanding 180,514,014 shares of common stock.

The holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of the stockholders. The holders of our common stock do not have any cumulative voting rights. Holders of our common stock are entitled to receive ratably any dividends declared by our board of directors out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding preferred stock. Our common stock has no preemptive rights, conversion rights or other subscription rights or redemption or sinking fund provisions.

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in all assets remaining after payment of all debts and other liabilities and any liquidation preference of any outstanding preferred stock. Each outstanding share of common stock is fully paid and non-assessable.

Undesignated Preferred Stock

As of December 31, 2025, no shares of our preferred stock were issued and outstanding.

Our board of directors has the authority, without further action by our stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon our liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our Company or other corporate action.

The existence of authorized but unissued shares of preferred stock may enable our board of directors to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our certificate of incorporation grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect

the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Registration Rights

Certain of our stockholders are entitled to rights with respect to the registration of securities under the Securities Act. These rights are provided under the terms of the Amended and Restated Investors' Rights Agreement between us, certain holders of our common stock and holders of our preferred stock dated as of August 13, 2021 (the "amended and restated investors' rights agreement"). The amended and restated investors' rights agreement includes demand registration rights, short-form registration rights and piggyback registration rights. All fees, costs and expenses of underwritten registrations under this agreement will be borne by us and all selling expenses, including underwriting discounts and selling commissions, will be borne by the holders of the shares being registered.

Demand Registration Rights

Certain stockholders are entitled to demand registration rights. Under the terms of the amended and restated investors' rights agreement, we will be required, upon the written request of holders of at least a majority of the registrable securities then outstanding to file a registration statement with respect to at least a majority of the registrable securities then outstanding, we will be required to file a registration statement within 60 days of such request covering all securities eligible for registration that our stockholders request to be included in such registration. We are required to effect only one registration pursuant to this provision of the amended and restated investors' rights agreement in any twelve-month period.

Short-form Registration Rights

Pursuant to the amended and restated investors' rights agreement, if we are eligible to file a registration statement on Form S-3, upon the written request of stockholders holding at least twenty percent of the securities eligible for registration then outstanding we will be required to file a Form S-3 registration restatement with respect to outstanding securities of such stockholders having an anticipated aggregate offering, net of related fees and expenses, of at least $3.0 million. We are required to effect only two registrations in any twelve month period pursuant to this provision of the amended and restated investors' rights agreement. The right to have such shares registered on Form S-3 is further subject to other specified conditions and limitations.

Piggyback Registration Rights

Pursuant to the amended and restated investors' rights agreement, if we register any of our securities either for our own account or for the account of other security holders, the holders of our common stock, including those issuable upon the conversion of our preferred stock, are entitled to include their shares in the registration. Subject to certain exceptions contained in the amended and restated investors' rights agreement, we and the underwriters may limit the number of shares included in the underwritten offering to the number of shares which we and the underwriters determine in our sole discretion will not jeopardize the success of the offering.

Indemnification

Our amended and restated investors' rights agreement contains customary cross-indemnification provisions, under which we are obligated to indemnify holders of registrable securities in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions attributable to them.

Expiration of Registration Rights

The demand registration rights and short form registration rights granted under the amended and restated investors' rights agreement will terminate on the earliest to occur of (a) the closing of certain liquidation events, (b) the fifth anniversary of the completion of our initial public offering or (c) at such time after our initial public offering when the holders' shares may be sold without restriction pursuant to Rule 144 under the Securities Act within a three month period.

Resale Registration Rights

In September 2024, we entered into a securities purchase agreement (the "Securities Purchase Agreement") with BMS, pursuant to which we agreed to prepare and file a registration statement with the SEC for purposes of registering the resale of 11,006,163 shares of our common stock held by BMS (the "BMS Shares").

Under the Securities Purchase Agreement, we agreed to use commercially reasonable efforts to cause such registration statement to be declared effective by the SEC as soon as practicable. Additionally, we agreed to maintain the effectiveness of the registration statement until the earliest to occur of: (i) the third (3rd) anniversary of the filing of the registration statement, (ii) the date that all of the BMS Shares covered by the registration statement have been sold pursuant to the registration statement, or (iii) such time as the BMS Shares become eligible for resale by non-affiliates of BMS without any volume limitations or other restrictions pursuant to Rule 144 under the Securities Act (including, for the avoidance of doubt, Rule 144(i)(2)) or any other rule of similar effect. We have agreed to be responsible for all fees and expenses incurred in connection with the registration of the BMS Shares.

In addition, pursuant to the terms of the Securities Purchase Agreement, BMS has agreed not to, directly or indirectly, sell or transfer any of the BMS Shares until September 30, 2027, subject to certain specified conditions and exceptions therein. We have also agreed, among other things, to indemnify BMS, its directors, officers, shareholders, members, partners, employees and agents, each other person, if any, who controls BMS and the directors, officers, shareholders, members, partners, employees and agents of each such controlling person from certain liabilities and to pay all fees and expenses incident to our obligations under the Securities Purchase Agreement. We filed the registration statement on Form S-3 covering the resale of the BMS Shares with the SEC on December 13, 2024, which became effective on December 20, 2024.

Expenses

Ordinarily, other than underwriting discounts and commissions, we are generally required to pay all expenses incurred by us related to any registration effected pursuant to the exercise of these registration rights. These expenses may include all registration and filing fees, printing expenses, fees and disbursements of our counsel, reasonable fees and disbursements of a counsel for the selling security holders and blue-sky fees and expenses.

Anti-takeover Effects of our Certificate of Incorporation and Bylaws and Delaware Law

Certain provisions of the Delaware General Corporation Law (the "DGCL") and of our certificate of incorporation and bylaws could have the effect of delaying, deferring or preventing another party from acquiring control of us and encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Board Composition and Filling Vacancies

Our certificate of incorporation provides for the division of our board of directors into three classes serving staggered three-year terms, with one class being elected each year. Our certificate of incorporation also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of two-thirds or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board of directors, may only be filled by the affirmative vote of a majority of our directors then in office even if less than a quorum. The classification of directors, together with the limitations on removal of directors and treatment of vacancies, has the effect of making it more difficult for stockholders to change the composition of our board of directors.

No Written Consent of Stockholders

Our certificate of incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting. This limit may lengthen the amount of time required to take stockholder actions and would

prevent the amendment of our bylaws or removal of directors by our stockholders without holding a meeting of stockholders.

Meetings of Stockholders

Our certificate of incorporation and bylaws provide that only a majority of the members of our board of directors then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our bylaws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

Advance Notice Requirements

Our bylaws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days nor more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. Our bylaws specify the requirements as to form and content of all stockholders' notices. These requirements may preclude stockholders from bringing matters before the stockholders at an annual or special meeting.

Amendment to Certificate of Incorporation and Bylaws

Any amendment of our certificate of incorporation must first be approved by a majority of our board of directors, and if required by law or our certificate of incorporation, must thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, board composition, limitation of liability and the amendment of our bylaws and certificate of incorporation must be approved by not less than two-thirds of the outstanding shares entitled to vote on the amendment, and not less than two-thirds of the outstanding shares of each class entitled to vote thereon as a class. Our bylaws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the bylaws; and may also be amended at an annual meeting of stockholders by the affirmative vote of at least two-thirds of the outstanding shares entitled to vote on the amendment, or, if our board of directors recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class.

Undesignated Preferred Stock

Our certificate of incorporation provides for 10,000,000 authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our certificate of incorporation grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Choice of Forum

Our bylaws provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for any state law claims 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, and employees to us or our stockholders, (3) any action asserting a claim arising pursuant to the DGCL, our certificate of incorporation or our bylaws (including the interpretation, validity or enforceability thereof) 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 that is governed by the internal affairs doctrine; provided, however, that the this provision shall not apply to any causes of action arising under the Securities Act, Exchange Act or to any claim for which the federal courts have exclusive jurisdiction. In addition, our bylaws provide that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States shall be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, the Exchange Act or the respective rules and regulations promulgated thereunder. To the fullest extent permitted by law, any person or entity purchasing or otherwise acquiring any interest in our securities shall be deemed to have notice of and consented to these forum provisions. These forum provisions may impose additional costs on stockholders, may limit our stockholders' ability to bring a claim in a forum they find favorable, and the designated courts may reach different judgments or results than other courts. In addition, there is uncertainty as to whether the federal forum provision for Securities Act claims will be enforced, which may impose additional costs on us and our stockholders.

Section 203 of the Delaware General Corporation Law

We are subject to the provisions of Section 203 of the DGCL. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, our board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances, but not the outstanding voting stock owned by the interested stockholder; or
- at or after the time the stockholder became interested, the business combination was approved by our board of directors and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, lease, pledge, exchange, mortgage or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; and
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges, or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

Listing on The Nasdaq Global Market

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

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A. The transfer agent and registrar's address is 150 Royall Street, Canton, MA 02021, and its telephone number is (781) 575-2000.

DESCRIPTION OF DEBT SECURITIES

We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. While the terms we have summarized below will apply generally to any debt securities that we may offer under this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. The terms of any debt securities offered under a prospectus supplement may differ from the terms described below. Unless the context requires otherwise, whenever we refer to the indenture, we also are referring to any supplemental indentures that specify the terms of a particular series of debt securities.

We will issue the debt securities under the indenture that we will enter into with the trustee named in the indenture. The indenture will be qualified under the Trust Indenture Act of 1939, as amended (the "Trust Indenture Act"). We have filed the form of indenture as an exhibit to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part, or will be incorporated by reference from, reports that we file with the SEC.

The following summary of material provisions of the debt securities and the indenture is subject to, and qualified in its entirety by reference to, all of the provisions of the indenture applicable to a particular series of debt securities. We urge you to read the applicable prospectus supplements and any related free writing prospectuses related to the debt securities that we may offer under this prospectus, as well as the complete indenture that contains the terms of the debt securities.

General

The indenture does not limit the amount of debt securities that we may issue. It provides that we may issue debt securities up to the principal amount that we may authorize and may be in any currency or currency unit that we may designate. Except for the limitations on consolidation, merger and sale of all or substantially all of our assets contained in the indenture, the terms of the indenture do not contain any covenants or other provisions designed to give holders of any debt securities protection against changes in our operations, financial condition or transactions involving us.

We may issue the debt securities issued under the indenture as "discount securities," which means they may be sold at a discount below their stated principal amount. These debt securities, as well as other debt securities that are not issued at a discount, may be issued with "original issue discount" ("OID") for U.S. federal income tax purposes because of interest payment and other characteristics or terms of the debt securities. Material U.S. federal income tax considerations applicable to debt securities issued with OID will be described in more detail in any applicable prospectus supplement.

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

- the title of the series of debt securities;
- any limit upon the aggregate principal amount that may be issued;
- the maturity date or dates;
- the form of the debt securities of the series;
- the applicability of any guarantees;
- whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;
- whether the debt securities rank as senior debt, senior subordinated debt, subordinated debt or any combination thereof, and the terms of any subordination;

- if the price (expressed as a percentage of the aggregate principal amount thereof) at which such debt securities will be issued is a price 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 or the method by which any such portion shall be determined;
- the interest rate or rates, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;
- our right, if any, to defer payment of interest and the maximum length of any such deferral period;
- if applicable, the date or dates after which, or the period or periods during which, and the price or prices at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;
- the date or dates, if any, on which, and the price or prices at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder's option to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;
- the denominations in which we will issue the series of debt securities, if other than denominations of $1,000 and any integral multiple thereof;
- any and all terms, if applicable, relating to any auction or remarketing of the debt securities of that series and any security for our obligations with respect to such debt securities and any other terms which may be advisable in connection with the marketing of debt securities of that series;
- whether the debt securities of the series shall be issued in whole or in part in the form of a global security or securities; the terms and conditions, if any, upon which such global security or securities may be exchanged in whole or in part for other individual securities; and the depositary for such global security or securities;
- if applicable, the provisions relating to conversion or exchange of any debt securities of the series and 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, the applicable conversion or exchange period and the manner of settlement for any conversion or exchange;
- if other than the full principal amount thereof, the portion of the principal amount of debt securities of the series which shall be payable upon declaration of acceleration of the maturity thereof;
- additions to or changes in the covenants applicable to the particular debt securities being issued, including, among others, the consolidation, merger or sale covenant;
- additions to or changes in the events of default with respect to the securities and any change in the right of the trustee or the holders to declare the principal, premium, if any, and interest, if any, with respect to such securities to be due and payable;
- additions to or changes in or deletions of the provisions relating to covenant defeasance and legal defeasance;
- additions to or changes in the provisions relating to satisfaction and discharge of the indenture;
- additions to or changes in the provisions relating to the modification of the indenture both with and without the consent of holders of debt securities issued under the indenture;

- the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars;
- 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;
- any restrictions on transfer, sale or assignment of the debt securities of the series; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, any other additions or changes in the provisions of the indenture, and any terms that may be required by us or advisable under applicable laws or regulations.

Conversion or Exchange Rights

We will set forth in the applicable prospectus supplement the terms on which a series of debt securities may be convertible into or exchangeable for our common stock or our other securities. We will include provisions as to settlement upon conversion or exchange and whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock or our other securities that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger or Sale

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the indenture will not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of our assets as an entirety or substantially as an entirety. However, any successor to or acquirer of such assets (other than any subsidiary of ours) must assume all of our obligations under the indenture or the debt securities, as appropriate.

Events of Default under the Indenture

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the following are events of default under the indenture with respect to any series of debt securities that we may issue:

- if we fail to pay any installment of interest on any series of debt securities, as and when the same shall become due and payable, and such default continues for a period of 90 days; provided, however, that a valid extension of an interest payment period by us in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of interest for this purpose;
- if we fail to pay the principal of, or premium, if any, on any series of debt securities as and when the same shall become due and payable whether at maturity, upon redemption, by declaration or otherwise, or in any payment required by any sinking or analogous fund established with respect to such series; provided, however, that a valid extension of the maturity of such debt securities in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of principal or premium, if any;
- if we fail to observe or perform any other covenant or agreement contained in the debt securities or the indenture, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive written notice of such failure, requiring the same to be remedied and stating that such is a notice of default thereunder, from the trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and
- if specified events of bankruptcy, insolvency or reorganization occur.

If an event of default with respect to debt securities of any series occurs and is continuing, other than an event of default specified in the last bullet point above, the trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series, by notice to us in writing, and to the trustee if notice is given by such holders, may declare the unpaid principal of, premium, if any, and accrued interest, if any, due and payable immediately. If an event of default specified in the last bullet point above occurs with respect to us, the principal amount of and accrued interest, if any, of each issue of debt securities then outstanding shall be due and payable without any notice or other action on the part of the trustee or any holder.

The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indenture, if an event of default under an indenture shall occur and be continuing, the trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the trustee reasonable indemnity. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, or exercising any trust or power conferred on the trustee, with respect to the debt securities of that series, provided that:

- the direction so given by the holder is not in conflict with any law or the applicable indenture; and
- subject to its duties under the Trust Indenture Act, the trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.
- A holder of the debt securities of any series will have the right to institute a proceeding under the indenture or to appoint a receiver or trustee, or to seek other remedies only if:
- the holder has given written notice to the trustee of a continuing event of default with respect to that series;
- the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made written request,
- such holders have offered to the trustee indemnity satisfactory to it against the costs, expenses and liabilities to be incurred by the trustee in compliance with the request; and
- the trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities.

We will periodically file statements with the trustee regarding our compliance with specified covenants in the indenture.

Modification of Indenture; Waiver

We and the trustee may change an indenture without the consent of any holders with respect to specific matters:

- to cure any ambiguity, defect or inconsistency in the indenture or in the debt securities of any series;
- to comply with the provisions described above under “Description of Debt Securities — Consolidation, Merger or Sale”;
- to provide for uncertificated debt securities in addition to or in place of certificated debt securities;

- to add to our covenants, restrictions, conditions or provisions such new covenants, restrictions, conditions or provisions for the benefit of the holders of all or any series of debt securities, 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 conferred upon us in the indenture;
- 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 indenture;
- to make any change that does not adversely affect the interests of any holder of debt securities of any series 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 above under "Description of Debt Securities — General" to establish the form of any certifications required to be furnished pursuant to the terms of the indenture or any series of debt securities, 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 any indenture by a successor trustee; or
- to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act.

In addition, under the indenture, the rights of holders of a series of debt securities may be changed by us and the trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series that is affected. However, unless we provide otherwise in the prospectus supplement 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 fixed maturity of any debt securities of any series;
- reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption of any series 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.

Discharge

Each indenture provides that we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for specified obligations, including obligations to:

- provide for payment;
- register the transfer or exchange of debt securities of the series;
- replace stolen, lost or mutilated debt securities of the series;
- pay principal of and premium and interest on any debt securities of the series;
- maintain paying agencies;
- hold monies for payment in trust;
- recover excess money held by the trustee;
- compensate and indemnify the trustee; and
- appoint any successor trustee.

In order to exercise our rights to be discharged, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, any premium, if any, and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we provide otherwise in the applicable prospectus supplement, in denominations of $1,000 and any integral multiple thereof. The indenture provides that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company ("DTC") or another depositary named by us and identified in the applicable prospectus supplement with respect to that series. To the extent the debt securities of a series are issued in global form and as book-entry, a description of terms relating to any book-entry securities will be set forth in the applicable prospectus supplement.

At the option of the holder, subject to the terms of the indenture and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indenture and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange, we will impose no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

If we elect to redeem the debt securities of any series, we will not be required to:

- issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or
- register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Trustee

The trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the trustee is under no obligation to exercise any of the powers given it by the indenture at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check that we will mail to the holder or by wire transfer to certain holders. Unless we otherwise indicate in the applicable prospectus supplement, we will designate the corporate trust office of the trustee as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the trustee for the payment of the principal of or any premium or interest on any debt securities that remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the debt security thereafter may look only to us for payment thereof.

Governing Law

The indenture 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 WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplements, summarizes the material terms and provisions of the warrants that we may offer under this prospectus and the related warrant agreements and warrant certificates. While the terms summarized below will apply generally to any warrants that we may offer, we will describe the particular terms of any series of warrants in more detail in the applicable prospectus supplement. If we indicate in the prospectus supplement, the terms of any warrants offered under that prospectus supplement may differ from the terms described below. Specific warrant agreements will contain additional important terms and provisions and will be incorporated by reference as an exhibit to the registration statement, which includes this prospectus.

General

We may issue warrants for the purchase of common stock, preferred stock and/or debt securities in one or more series. We may issue warrants independently or together with common stock, preferred stock and/or debt securities, and the warrants may be attached to or separate from these securities.

We will evidence each series of warrants by warrant certificates that we will issue under a separate warrant agreement. We will enter into the warrant agreement with a warrant agent. We will indicate the name and address of the warrant agent in the applicable prospectus supplement relating to a particular series of warrants.

We will describe in the applicable prospectus supplement the terms of the series of warrants, including:

- the offering price and aggregate number of warrants offered;
- the currency for which the warrants may be purchased;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;
- if applicable, the date on and after which the warrants and the related securities will be separately transferable;
- in the case of warrants to purchase common stock or preferred stock, the number of shares of common stock or preferred stock, as the case may be, purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;
- in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at, and currency in which, this principal amount of debt securities may be purchased upon such exercise;
- the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreement and the warrants;
- the terms of any rights to redeem or call the warrants;
- any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;
- the periods during which, and places at which, the warrants are exercisable;
- the manner of exercise;
- the dates on which the right to exercise the warrants will commence and expire;
- the manner in which the warrant agreement and warrants may be modified;
- federal income tax consequences of holding or exercising the warrants;

- the terms of the securities issuable upon exercise of the warrants; and
- any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

DESCRIPTION OF UNITS

We may issue units comprised of shares of common stock, shares of preferred stock, debt securities and warrants in any combination. We may issue units in such amounts and in as many distinct series as we wish. This section outlines certain provisions of the units that we may issue. If we issue units, they will be issued under one or more unit agreements to be entered into between us and a bank or other financial institution, as unit agent. The information described in this section may not be complete in all respects and is qualified entirely by reference to the unit agreement with respect to the units of any particular series. The specific terms of any series of units offered will be described in the applicable prospectus supplement. If so described in a particular supplement, the specific terms of any series of units may differ from the general description of terms presented below. We urge you to read any prospectus supplement related to any series of units we may offer, as well as the complete unit agreement and unit certificate that contain the terms of the units. If we issue units, forms of unit agreements and unit certificates relating to such units will be incorporated by reference as exhibits to the registration statement, which includes this prospectus.

Each unit that we may issue 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. The applicable prospectus supplement may describe:

- the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any provisions of the governing unit agreement;
- the price or prices at which such units will be issued;
- the applicable United States federal income tax considerations relating to the units;
- any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units; and
- any other terms of the units and of the securities comprising the units.

The provisions described in this section, as well as those described under “Description of Capital Stock,” “Description of Debt Securities” and “Description of Warrants” will apply to the securities included in each unit, to the extent relevant and as may be updated in any prospectus supplements.

Issuance in Series

We may issue units in such amounts and in as many distinct series as we wish. This section summarizes terms of the units that apply generally to all series. Most of the financial and other specific terms of a particular series of units will be described in the applicable prospectus supplement.

Unit Agreements

We will issue the units under one or more unit agreements to be entered into between us and a bank or other financial institution, as unit agent. We may add, replace or terminate unit agents from time to time. We will identify the unit agreement under which each series of units will be issued and the unit agent under that agreement in the applicable prospectus supplement.

The following provisions will generally apply to all unit agreements unless otherwise stated in the applicable prospectus supplement:

Modification without Consent

We and the applicable unit agent may amend any unit or unit agreement without the consent of any holder:

- to cure any ambiguity; any provisions of the governing unit agreement that differ from those described below;
- to correct or supplement any defective or inconsistent provision; or
- to make any other change that we believe is necessary or desirable and will not adversely affect the interests of the affected holders in any material respect.

We do not need any approval to make changes that affect only units to be issued after the changes take effect. We may also make changes that do not adversely affect a particular unit in any material respect, even if they adversely affect other units in a material respect. In those cases, we do not need to obtain the approval of the holder of the unaffected unit; we need only obtain any required approvals from the holders of the affected units.

Modification with Consent

We may not amend any particular unit or a unit agreement with respect to any particular unit unless we obtain the consent of the holder of that unit, if the amendment would:

- impair any right of the holder to exercise or enforce any right under a security included in the unit if the terms of that security require the consent of the holder to any changes that would impair the exercise or enforcement of that right; or
- reduce the percentage of outstanding units or any series or class the consent of whose holders is required to amend that series or class, or the applicable unit agreement with respect to that series or class, as described below.

Any other change to a particular unit agreement and the units issued under that agreement would require the following approval:

- If the change affects only the units of a particular series issued under that agreement, the change must be approved by the holders of a majority of the outstanding units of that series; or
- If the change affects the units of more than one series issued under that agreement, it must be approved by the holders of a majority of all outstanding units of all series affected by the change, with the units of all the affected series voting together as one class for this purpose.

These provisions regarding changes with majority approval also apply to changes affecting any securities issued under a unit agreement, as the governing document.

In each case, the required approval must be given by written consent.

Unit Agreements Will Not Be Qualified under Trust Indenture Act

No unit agreement will be qualified as an indenture, and no unit agent will be required to qualify as a trustee, under the Trust Indenture Act. Therefore, holders of units issued under unit agreements will not have the protections of the Trust Indenture Act with respect to their units.

Mergers and Similar Transactions Permitted; No Restrictive Covenants or Events of Default

The unit agreements will not restrict our ability to merge or consolidate with, or sell our assets to, another corporation or other entity or to engage in any other transactions. If at any time we merge or consolidate with, or sell our assets substantially as an entirety to, another corporation or other entity, the successor entity will succeed to and assume our obligations under the unit agreements. We will then be relieved of any further obligation under these agreements.

The unit agreements will not include any restrictions on our ability to put liens on our assets, nor will they restrict our ability to sell our assets. The unit agreements also will not provide for any events of default or remedies upon the occurrence of any events of default.

Governing Law

The unit agreements and the units will be governed by New York law.

Form, Exchange and Transfer

We will issue each unit in global—i.e., book-entry—form only. Units in book-entry form will be represented by a global security registered in the name of a depositary, which will be the holder of all the units represented by the global security. Those who own beneficial interests in a unit will do so through participants in the depositary's system, and the rights of these indirect owners will be governed solely by the applicable procedures of the depositary and its participants. We will describe book-entry securities, and other terms regarding the issuance and registration of the units in the applicable prospectus supplement.

Each unit and all securities comprising the unit will be issued in the same form.

If we issue any units in registered, non-global form, the following will apply to them.

The units will be issued in the denominations stated in the applicable prospectus supplement. Holders may exchange their units for units of smaller denominations or combined into fewer units of larger denominations, as long as the total amount is not changed.

- Holders may exchange or transfer their units at the office of the unit agent. Holders may also replace lost, stolen, destroyed or mutilated units at that office. We may appoint another entity to perform these functions or perform them ourselves.
- Holders will not be required to pay a service charge to transfer or exchange their units, but they may be required to pay for any tax or other governmental charge associated with the transfer or exchange. The transfer or exchange, and any replacement, will be made only if our transfer agent is satisfied with the holder's proof of legal ownership. The transfer agent may also require an indemnity before replacing any units.
- If we have the right to redeem, accelerate or settle any units before their maturity, and we exercise our right as to less than all those units or other securities, we may block the exchange or transfer of those units during the period beginning 15 days before the day we mail the notice of exercise and ending on the day of that mailing, in order to freeze the list of holders to prepare the mailing. We may also refuse to register transfers of or exchange any unit selected for early settlement, except that we will continue to permit transfers and exchanges of the unsettled portion of any unit being partially settled. We may also block the transfer or exchange of any unit in this manner if the unit includes securities that are or may be selected for early settlement.

Only the depositary will be entitled to transfer or exchange a unit in global form, since it will be the sole holder of the unit.

Payments and Notices

In making payments and giving notices with respect to our units, we will follow the procedures as described in the applicable prospectus supplement.

MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS FOR NON-U.S. HOLDERS

The following discussion is a summary of certain material U.S. federal income tax considerations applicable to non-U.S. holders (as defined below) with respect to their ownership and disposition of shares of our common stock issued pursuant to this offering. For purposes of this discussion, a non-U.S. holder means a beneficial owner of our common stock that is for U.S. federal income tax purposes:

- a non-resident alien individual;
- a foreign corporation or other foreign organization taxable as a corporation; or
- a foreign trust or estate the income of which is not subject to U.S. federal income tax on a net income basis.

This discussion does not address the tax treatment of partnerships or other entities that are pass-through entities for U.S. federal income tax purposes or persons that hold their common stock through partnerships or other pass-through entities. A partner in a partnership or other pass-through entity that will hold our common stock should consult his, her or its tax advisor regarding the tax consequences of acquiring, holding and disposing of our common stock through a partnership or other pass-through entity, as applicable.

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended (the "Code"), existing and proposed U.S. Treasury Regulations promulgated thereunder, current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus and, all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any such change or differing interpretation could alter the tax consequences to non-U.S. holders described in this prospectus. There can be no assurance that the Internal Revenue Service (the "IRS"), will not challenge one or more of the tax consequences described herein. We assume in this discussion that a non-U.S. holder holds shares of our common stock as a capital asset within the meaning of Section 1221 of the Code, generally property held for investment.

This discussion does not address all aspects of U.S. federal income taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder's individual circumstances nor does it address any aspects of U.S. state, local or non-U.S. taxes, the alternative minimum tax, the Medicare contribution tax on net investment income, the rules regarding qualified small business stock within the meaning of Section 1202 of the Code, or any other aspect of any U.S. federal tax other than income taxes. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as:

- insurance companies;
- tax-exempt or governmental organizations;
- financial institutions;
- brokers or dealers in securities;
- "regulated investment companies" and "real estate investment trusts";
- pension plans;
- "controlled foreign corporations," "passive foreign investment companies," and corporations that accumulate earnings to avoid U.S. federal income tax;
- "qualified foreign pension funds," or entities wholly owned by a "qualified foreign pension fund";
- partnerships or other entities or arrangements treated as partnerships for U.S. federal income tax purposes (and partners and investors therein);
- persons deemed to sell our common stock under the constructive sale provisions of the Code;

- persons that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment; and
- U.S. expatriates.

This discussion is for general information only and is not tax advice. Accordingly, all prospective non-U.S. holders of our common stock should consult their tax advisors with respect to the U.S. federal, state, local and non-U.S. tax consequences of the purchase, ownership and disposition of our common stock.

Distributions of Our Common Stock

We have never declared or paid any cash distributions on our capital stock and we do not anticipate paying cash distributions on our common stock for the foreseeable future. Distributions, if any, on our common stock will generally constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder's investment, up to such holder's tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below in "Gain on Sale or Other Taxable Disposition of Our Common Stock." Any such distributions will also be subject to the discussions below under the sections entitled "Backup Withholding and Information Reporting" and "Withholding and Information Reporting Requirements-FATCA."

Subject to the discussion in the following two paragraphs in this section, dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a 30 percent rate or a reduced rate specified by an applicable income tax treaty between the United States and such holder's country of residence.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30 percent withholding tax if the non-U.S. holder satisfies applicable certification requirements. However, such U.S. effectively connected income, net of specified deductions and credits, is taxed at the same graduated U.S. federal income tax rates applicable to United States persons (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is a corporation may also, under certain circumstances, be subject to an additional "branch profits tax" at a 30 percent rate or a reduced rate specified by an applicable income tax treaty between the United States and such holder's country of residence.

A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder's country of residence generally will be required to provide a properly executed IRS Form W-8BEN or W-8BEN-E (or other applicable or successor form) to the applicable withholding agent and satisfy applicable certification and other requirements. Any documentation provided to an applicable withholding agent may need to be updated in certain circumstances. Non-U.S. holders are urged to consult their tax advisors regarding their entitlement to benefits under a relevant income tax treaty. A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim with the IRS.

Gain on Sale or Other Taxable Disposition of Our Common Stock

Subject to the discussions below under "Backup Withholding and Information Reporting" and "Withholding and Information Reporting Requirements-FATCA," a non-U.S. holder generally will not be subject to any U.S. federal income or withholding tax on any gain realized upon such holder's sale or other taxable disposition of shares of our common stock unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a U.S. trade or business and, if an applicable income tax treaty so provides, is attributable to a permanent establishment or a fixed base maintained by such non-U.S. holder in the United States, in which case the non-U.S. holder generally will be taxed on a net income basis at the graduated U.S. federal income tax rates applicable to United States

persons (as defined in the Code) and, if the non-U.S. holder is a foreign corporation, the branch profits tax described above in "Distributions on Our Common Stock" also may apply;

- the non-U.S. holder is a nonresident alien individual who is present in the United States for a period or periods aggregating 183 days or more in the taxable year of the disposition and certain other conditions are met, in which case the non-U.S. holder will be subject to a 30 percent tax (or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence) on the net gain derived from the disposition, which may be offset by certain U.S. source capital losses of the non-U.S. holder, if any (even though the individual is not considered a resident of the United States), provided that the non-U.S. holder has timely filed U.S. federal income tax returns with respect to such losses; or

- we are, or have been, at any time during the five-year period preceding such sale or other taxable disposition (or the non-U.S. holder's holding period, if shorter) a "U.S. real property holding corporation," as described below, unless our common stock is regularly traded on an established securities market and the non-U.S. holder holds no more than 5 percent of our outstanding common 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 our common stock. Generally, a corporation is a U.S. real property holding corporation if the fair market value of its U.S. real property interests, as defined in the Code and applicable Treasury regulations, equals or exceeds 50 percent of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we do not believe that we are, or have been, a U.S. real property holding corporation, or that we are likely to become one in the future. No assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rules described above.

Backup Withholding and Information Reporting

We (or the applicable paying agent) must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock paid to such holder and the tax withheld, if any, with respect to such distributions. A non-U.S. holder may have to comply with specific certification procedures to establish that the holder is not a United States person (as defined in the Code) in order to avoid backup withholding at the applicable rate with respect to dividends on our common stock. Dividends paid to non-U.S. holders subject to withholding of U.S. federal income tax, as described above in "Distributions on Our Common Stock," generally will be exempt from U.S. backup withholding.

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

Non-U.S. holders should consult their tax advisors regarding the application of the information reporting and backup withholding rules to them. Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement. Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that an appropriate claim is filed with the IRS in a timely manner.

Withholding and Information Reporting Requirements - FATCA

Provisions of the Code commonly referred to as the Foreign Account Tax Compliance Act ("FATCA") generally impose a U.S. federal withholding tax at a rate of 30 percent on payments of dividends on, or, subject to the

discussion of certain proposed U.S. Treasury regulations below, gross proceeds from the sale or other disposition of, our common stock paid to a foreign entity unless (i) if the foreign entity is a "foreign financial institution," such foreign entity undertakes certain due diligence, reporting, withholding, and certification obligations, (ii) if the foreign entity is not a "foreign financial institution," such foreign entity identifies certain of its U.S. investors, if any, or (iii) the foreign entity is otherwise exempt under FATCA. However, the U.S. Treasury released proposed regulations which, if finalized in their present form, would eliminate the federal withholding tax of 30 percent applicable to the gross proceeds of a sale or other disposition of our common stock. In the preamble to such proposed regulations, the U.S. Treasury stated that taxpayers (including withholding agents) may generally rely on the proposed regulations until final regulations are issued. Under certain circumstances, a non-U.S. holder may be eligible for refunds or credits of this withholding tax. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this paragraph. Non-U.S. holders should consult their tax advisors regarding the possible implications of this legislation on their investment in our common stock and the entities through which they hold our common stock, including, without limitation, the process and deadlines for meeting the applicable requirements to prevent the imposition of the 30 percent withholding tax under FATCA.

PLAN OF DISTRIBUTION

We may sell the securities offered through this prospectus and any accompanying prospectus supplement, if required, in any of the following ways: (i) to or through underwriters or dealers, (ii) directly to purchasers, including our affiliates, (iii) through agents, (iv) in an "at the market offering," within the meaning of Rule 415(a)(4) of the Securities Act or (v) through a combination of any of these methods or any other method permitted by law. The securities may be distributed at a fixed price or prices, which may be changed, market prices prevailing at the time of sale, prices related to the prevailing market prices, or negotiated prices, either:

- on or through the facilities of The Nasdaq Global Market or any other securities exchange or quotation or trading service on which such securities may be listed, quoted or traded at the time of sale; and/or
- to or through a market maker otherwise than on The Nasdaq Global Market or such other securities exchanges or quotation or trading services.

In addition, we may issue the securities as a dividend or distribution or in a subscription rights offering to our existing security holders.

We may directly solicit offers to purchase securities, or agents may be designated to solicit such offers. In the prospectus supplement relating to such offering, we will name any agent that could be viewed as an underwriter under the Securities Act and describe any commissions that we must pay to any such agent. 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. 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.

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;
- any discounts and commissions to be allowed or paid to the agent or underwriters;
- all other items constituting underwriting compensation;
- any discounts and commissions to be allowed or paid to dealers; and
- any exchanges on which the securities will be listed.

If any underwriters or agents are used in the sale of the securities in respect of which this prospectus is delivered, we will enter into an underwriting agreement, sales 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.

In connection with the offering of securities, we may grant to the underwriters an option to purchase additional securities with an additional underwriting commission, as may be set forth in the accompanying prospectus supplement. If we grant any such option, the terms of such option will be set forth in the prospectus supplement for such securities.

If a dealer is used in the sale of the securities in respect of which the prospectus is delivered, we will sell such securities to the dealer, as principal. The dealer, who may be deemed to be an "underwriter" as that term is defined in the Securities Act, 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.

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.

Offered securities may also be offered and sold, if so indicated in the prospectus supplement, in connection with a remarketing upon their purchase, in accordance with a redemption or repayment pursuant to their terms, or otherwise, by one or more remarketing firms, acting as principals for their own accounts or as agents for us. Any remarketing firm will be identified and the terms of its agreement, if any, with us and its compensation will be described in the applicable prospectus supplement. Remarketing firms may be deemed to be underwriters in connection with their remarketing of offered securities.

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

Certain underwriters may use this prospectus and any accompanying prospectus supplement for offers and sales related to market-making transactions in the securities. These underwriters may act as principal or agent in these transactions, and the sales will be made at prices related to prevailing market prices at the time of sale. Any underwriters involved in the sale of the securities may qualify as "underwriters" within the meaning of Section 2(a)(11) of the Securities Act. In addition, the underwriters' commissions, discounts or concessions may qualify as underwriters' compensation under the Securities Act and the rules of the Financial Industry Regulatory Authority.

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 overallot in connection with the offering, creating a short position for their own accounts. In addition, to cover overallotments 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.

We may engage in at the market offerings into an existing trading market in accordance with Rule 415(a)(4) under the Securities Act. In addition, we may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement so indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter and, if not identified in this prospectus, will be named in the applicable prospectus supplement (or a post-effective amendment). In addition, we may otherwise loan or pledge securities to a financial institution or other third party that in turn may sell the securities short using this prospectus and an applicable prospectus supplement. Such financial institution or other third party may transfer its economic short position to investors in our securities or in connection with a concurrent offering of other securities.

Under Rule 15c6-1 of the Exchange Act, trades in the secondary market generally are required to settle in one business day, 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 one scheduled business day after the trade date for your securities. Accordingly, in such a case, if you wish to trade securities on any date prior to the first business day before the original issue date for your securities, you will be required, by virtue of the fact that your securities initially are expected to settle in more than one scheduled business day 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.

The specific terms of any lock-up provisions in respect of any given offering will be described in the applicable prospectus supplement.

Any underwriters, dealers and agents may engage in transactions with us, or perform services for us, in the ordinary course of business for which they receive compensation.

The anticipated date of delivery of offered securities will be set forth in the applicable prospectus supplement relating to each offer.

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, Boston, Massachusetts. Any underwriters will also be advised about the validity of the securities and other legal matters by their own counsel, which will be named in the prospectus supplement.

EXPERTS

The financial statements incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2025 have been so incorporated in reliance on the report (which contains an explanatory paragraph relating to the Company's ability to continue as a going concern as described in Note 1 to the financial statements) of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

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 www.sec.gov and on our website at *www.primemedicine.com*. Information contained in, or that can be accessed through, our website is not a part of this prospectus and is not incorporated by reference in this prospectus.

We have the authority to designate and issue more than one class or series of stock having various preferences, conversion and other rights, voting powers, restrictions, limitations as to dividends, qualifications, and terms and conditions of redemption. See "Description of Capital Stock." We will furnish a full statement of the relative rights and preferences of each class or series of our stock which has been so designated and any restrictions on the ownership or transfer of our stock to any stockholder upon request and without charge. Written requests for such copies should be directed to Prime Medicine, Inc., 60 First Street, Cambridge, MA 02141.

This prospectus is part of a shelf registration statement on Form S-3 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 subsidiaries and the securities we are offering. Statements in this prospectus concerning any document we filed as an exhibit to the registration statement or that we otherwise filed with the SEC are not intended to be comprehensive and are qualified by reference to these filings. You should review the complete document to evaluate these statements.

INCORPORATION 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, which we have already filed with the SEC (Commission File No. 001-41536), and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, including all filings made after the date of the filing of this registration statement and prior to the effectiveness of this registration statement, except as to any portion of any future report or document that is not deemed filed under such provisions, until we sell all of the securities:

- Annual Report on Form 10-K for the fiscal year ended December 31, 2025, filed with the SEC on March 3, 2026; and
- The description of our common stock contained in our Registration Statement on Form 8-A (File No. 001-41536) as filed with the SEC on October 17, 2022, including any amendments or reports filed for the purpose of updating such description, including Exhibit 4.3 to our Annual Report on Form 10-K for the year ended December 31, 2025, as filed with the SEC on March 3, 2026.

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

Prime Medicine, Inc.
60 First Street
Cambridge, MA 02141
(617) 465-0013

You may also access these documents, free of charge on the SEC's website at www.sec.gov or on our website at www.primemedicine.com. Information contained in or accessible through our website does not constitute a part of this prospectus and is not incorporated by reference in this prospectus. We have included our website solely as an inactive textual reference.

Notwithstanding the foregoing, unless specifically stated to the contrary, information that we furnish (and that is not deemed "filed" with the SEC) under Items 2.02 and 7.01 of any Current Report on Form 8-K, including the related exhibits under Item 9.01, is not incorporated by reference into this prospectus or the registration statement of which this prospectus is a part.

This prospectus is part of a registration statement we filed with the SEC. We have incorporated exhibits into this registration statement. You should read the exhibits carefully for provisions that may be important to you.

You should rely only on the information incorporated by reference or provided in this prospectus or any prospectus supplement. We have not authorized anyone to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus or in the documents incorporated by reference is accurate as of any date other than the date on the front of this prospectus or those documents.

$125,000,000



Common Stock

PROSPECTUS SUPPLEMENT

Joint Book-Running Managers

Jefferies **TD Cowen** **Goldman Sachs & Co. LLC**

Passive Book-Running Managers

Oppenheimer & Co. **LifeSci Capital**

, 2026