Issuer Free Writing Prospectus
Filed Pursuant to Rule 433
Dated February 14, 2024
Relating to Preliminary Prospectus Supplement Dated February 14, 2024
Registration Statement No. 333-275321



Common Stock

Pre-funded Warrants to Purchase Shares of Common Stock

This free writing prospectus relates only to the public offering of shares of common stock and pre-funded warrants to purchase shares of common stock by Prime Medicine, Inc. and should be read together with the preliminary prospectus supplement dated February 14, 2024 (the "Preliminary Prospectus Supplement"), and the accompanying base prospectus, in each case, including the documents incorporated by reference therein. The information in this free writing prospectus updates and, to the extent inconsistent, supersedes the information in the Preliminary Prospectus Supplement. This free writing prospectus supplements the Preliminary Prospectus Supplement primarily to reflect the addition of certain pre-funded warrants, and the shares of common stock issuable upon the exercise of such pre-funded warrants, to the securities being offered by Prime Medicine, Inc. in this offering. Except as otherwise indicated, all information in this free writing prospectus and the Preliminary Prospectus Supplement assumes no exercise by the underwriters of their option to purchase additional shares of common stock and no exercise of the pre-funded warrants included in this offering.

This free writing prospectus is qualified in its entirety by reference to the Preliminary Prospectus Supplement and the accompanying base prospectus, in each case, including the documents incorporated by reference therein. Financial information and other information presented in the Preliminary Prospectus Supplement or incorporated by reference therein is deemed to have changed to the extent affected by the changes described herein. This free writing prospectus should be read together with the Preliminary Prospectus Supplement and the accompanying base prospectus, in each case, including the documents incorporated by reference therein, before making a decision in connection with an investment in the securities. Capitalized terms used in this free writing prospectus but not defined have the meanings given to them in the Preliminary Prospectus Supplement.

Common stock we are offering pursuant to this prospectus supplement

\$140,000,000 of shares.

Pre-funded warrants offered by us

We are also offering, in lieu of common stock, to certain investors who so choose, pre-funded warrants to purchase shares of our common stock. The purchase price of each pre-funded warrant will equal the price per share at which the shares of our common stock are being sold to the public in this offering, minus \$0.00001, which is the exercise price of each pre-funded warrant per share. The pre-funded warrants do not expire, and each pre-funded warrant will be exercisable at any time after the date of issuance of such pre-funded warrant, subject to an ownership limitation. See "Description of Pre-Funded Warrants." This free writing prospectus and the Preliminary Prospectus Supplement also relate to the offering of the shares of our common stock issuable upon the exercise of such pre-funded warrants.

The lock-up restrictions described in the Preliminary Prospectus Supplement under "Underwriting" will not apply to issuance of common stock upon the exercise of the pre-funded warrants during the 90-day period following the date of the final prospectus supplement to be filed in connection with this offering.

Option to purchase additional shares from

We have granted the underwriters an option for a period of 30 days from the date of this prospectus supplement to purchase up to \$21,000,000 of additional shares of our common stock. The number of shares subject to the underwriters' option equals 15% of the total number of shares of common stock we are offering plus the shares of common stock underlying the pre-funded warrants.

Use of proceeds

We estimate that the net proceeds to us from this offering will be approximately \$131.2 million, or approximately \$150.9 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, short-term investments, and related party short-term investments, primarily to fund research and development and clinical development to support the advancement of current or future product candidates and the expansion of our research and development programs, and the remainder for working capital, capital expenditures and other general corporate purposes. See "Use of Proceeds."

Nasdaq Global Market symbol

Our shares of common stock are listed on the Nasdaq Global Market under the symbol "PRME." We do not intend to list the pre-funded warrants on the Nasdaq Global Market or any other national securities exchange or any recognized trading system. Without an active market, the liquidity of the pre-funded warrants will be limited. See "Description of Pre-Funded Warrants."

RISK FACTORS

If you purchase securities in this offering, you will experience immediate and substantial dilution in the book value of your shares.

If you purchase shares of our common stock or pre-funded warrants in this offering, you will incur immediate and substantial dilution in the as adjusted net tangible book value of your common stock or the underlying pre-funded warrants purchased in this offering 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 titled "Dilution."

The pre-funded warrants are not listed on any exchange and we do not intend to list the pre-funded warrants on any exchange.

If you purchase pre-funded warrants, you may be unable to sell such warrants at the prices desired or at all. There is no existing trading market for the pre-funded warrants and there can be no assurance that a liquid market will develop or be maintained for the pre-funded warrants, or that you will be able to sell any of the pre-funded warrants at a particular time (if at all). In addition, we do not intend to apply for listing of the pre-funded warrants on Nasdaq or any other securities exchange or nationally recognized trading system. The liquidity of the trading market in the pre-funded warrants and the sale price, if any, for the pre-funded warrants, may be adversely affected by, among other things: (i) changes in the overall market for the pre-funded warrants; (ii) changes in our financial performance or prospects; (iii) changes or perceived changes in our creditworthiness; (iv) the prospects for companies in the industry generally; (v) the number of holders of the pre-funded warrants; and (vi) the interest of securities dealers in making a market for the pre-funded warrants.

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

Until holders of the pre-funded warrants exercise their pre-funded warrants and acquire shares of our common stock, such holders will have no rights with respect to the shares of our common stock underlying such pre-funded warrants, except that the holder of a pre-funded warrant shall be entitled to participate in certain distributions, including cash dividends, if any, to all holders of our common stock for no consideration. Upon exercise of their respective pre-funded warrants, the holders will be entitled to exercise the rights of a common stockholder only as to matters for which the record date occurs after the exercise date.

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

A holder of the pre-funded warrants will not be entitled to exercise any portion of such pre-funded warrants which, upon giving effect to such exercise, would cause (i) the aggregate number of shares of our common stock beneficially owned by the holder (together with its affiliates) to exceed 4.99% of the total number of shares of our common stock outstanding immediately after giving effect to the exercise, or (ii) the combined voting power of our securities beneficially owned by such holder (together with its affiliates and other attribution parties) to exceed 4.99% of the combined voting power of all of our securities then outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the pre-funded warrants. Such percentage may be increased by the holder of the pre-funded warrants to any other percentage not in excess of 19.99% upon at least 61 days' prior notice from the holder to us. As a result, you may not be able to exercise your pre-funded warrants for shares of our common stock at a time when it would be financially beneficial for you to do so. In such circumstance you could seek to sell your pre-funded warrants to realize value, but you may be unable to do so in the absence of an established trading market for the pre-funded warrants.

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

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

If we do not maintain a current and effective registration statement relating to the share of common stock issuable upon exercise of the pre-funded warrants, holders will only be able to exercise such pre-funded warrants on a "cashless basis."

If we do not maintain a current and effective registration statement relating to the shares of common stock issuable upon exercise of the pre-funded warrants at the time that holders wish to exercise such pre-funded warrants, they will only be able to exercise them on a "cashless basis" provided that an exemption from registration is available. As a result, the number of ordinary shares that holders will receive upon exercise of the pre-funded warrants will be fewer than it would have been had such holder exercised his warrant for cash, and holders may be limited in their ability to immediately sell shares upon exercise subject to volume or other securities law limitations. Further, if an exemption from registration is not available, holders would not be able to exercise on a cashless basis and would only be able to exercise their pre-funded warrants for cash if a current and effective registration statement relating to the shares of common stock issuable upon exercise of the pre-funded warrants is available.

USE OF PROCEEDS

We estimate that the net proceeds from this offering will be approximately \$131.2 million, or approximately \$150.9 million if the underwriters exercise in full their option to purchase additional shares, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. We will receive nominal proceeds, if any, from any exercise of pre-funded warrants.

We currently intend to use the net proceeds from this offering, together with our existing cash, cash, short-term investments, and related party short-term investments, to primarily fund research and development and clinical development to support the advancement of our current or future product candidates and the expansion of our research and development programs, 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. 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 or pre-funded warrants 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 or prefunded warrant and the as adjusted net tangible book value per share of our common stock after this offering.

As of September 30, 2023, we had net tangible book value of approximately \$194.0 million, or \$1.99 per share of our common stock, based upon 97,324,301 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.

Without taking into account any other changes in our historical net tangible book value after September 30, 2023, other than to give effect to the issuance and sale of shares of our common stock in this offering at the public offering price of \$ per share, and pre-funded warrants to purchase shares of common stock at the public offering price of \$ per pre-funded warrant (which equals the public offering price of the common stock at which shares of our common stock are being sold to the public in this offering less the \$0.00001 per share exercise price of each such pre-funded warrant) (excluding shares of common stock issuable upon exercise of the pre-funded warrants, any proceeds which may be received upon exercise of the prefunded warrants or any resulting accounting associated with the exercise of the pre-funded warrants), and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2023 would have been \$ million, or \$ per share. This represents an immediate increase of \$ in as adjusted net tangible book value per share to existing stockholders and immediate dilution of \$ in as adjusted net tangible book value per share to investors purchasing shares of our common stock or pre-funded warrants in this offering from the public offering price per share paid by investors purchasing shares of our common stock or pre-funded warrants in this offering from the public offering price per share paid by investors purchasing shares of our common stock or pre-funded warrants in this offering from the public offering price per share basis:

| Public offering price per share | \$ |
|---|------------|
| Historical net tangible book value per share as of September 30, 2023 | \$ 1.99 |
| Increase in as-adjusted 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 new investors in this offering | \$ |

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

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

The above discussion and table are based on 97,324,301 shares of our common stock outstanding as of September 30, 2023 excludes:

- 7,634,966 shares of common stock issuable upon the exercise of stock options outstanding as of September 30, 2023, at a weighted average exercise price of \$9.70 per share;
- 1,262,000 shares of common stock issuable upon the vesting of restricted common stock outstanding as of September 30, 2023;
- 8,805,586 shares of common stock available for future issuance under our 2022 Stock Option and Incentive Plan as of September 30, 2023, as well as any increases in the number of shares of common stock reserved for issuance thereunder; and

• 1,942,700 shares of common stock available for future issuance under our 2022 Employee Stock Purchase Plan as of September 30, 2023, 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 \$21,000,000 of 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 additional shares of common stock are issued pursuant to the Sales Agreement with Jefferies LLC, 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.

DESCRIPTION OF PRE-FUNDED WARRANTS

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

Form

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

Term

The pre-funded warrants do not expire.

Exercisability

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

Exercise Limitations

We may not effect the exercise of any pre-funded warrant, and a holder will not be entitled to exercise any portion of any pre-funded warrant that, upon giving effect to such exercise, would cause the aggregate number of shares of our common stock beneficially owned by the holder (together with its attribution affiliates (as defined below)) to exceed 4.99% of the number of shares of our common stock that would be outstanding immediately after giving effect to the exercise. However, any holder of a pre-funded warrant may increase or decrease such percentage to any other percentage not in excess of 19.99% upon at least 61 days' prior notice from the holder to us. For purposes of the foregoing, "attribution affiliates" means, collectively, the following persons and entities with respect to any holder: (i) its direct or indirect affiliates, (ii) any person acting or who could be deemed to be acting as a Section 13(d) "group" together with the holder or any attribution parties and (iii) any other persons whose beneficial ownership of our common stock would or could be aggregated with the holder and/or any other attribution parties for purposes of Section 13(d) or Section 16 of the Securities Exchange Act of 1934, as amended.

Exercise Price

The exercise price per whole share of our common stock purchasable upon the exercise of the pre-funded warrants is \$0.00001 per share of common stock. The exercise price of the pre-funded warrants and the number of shares of our common stock issuable upon exercise of the pre-funded warrants is subject to appropriate adjustment in the event of certain stock dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting our common stock.

Transferability

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

Exchange Listing

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

Fundamental Transactions

In the event of a fundamental transaction, as described in the pre-funded warrants and generally including any reorganization, recapitalization or reclassification of our common stock, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, the acquisition of more than 50% of our outstanding common stock, or any person or group becoming the beneficial owner of more than 50% of the voting power represented by our outstanding common stock, the holders of the pre-funded warrants will be entitled to receive upon exercise of the pre-funded warrants the kind and amount of securities, cash or other property that the holders would have received had they exercised the pre-funded warrants immediately prior to such fundamental transaction without regard to any limitations on exercise contained in the pre-funded warrants.

Rights as a Stockholder

Except for the right to participate in certain dividends and distributions and as otherwise provided in the pre-funded warrants or by virtue of a holder's ownership of shares of our common stock, the holder of a pre-funded warrant does not have the rights or privileges of a holder of our common stock, including any voting rights, until the holder exercises the pre-funded warrant.

UNDERWRITING

The underwriters will purchase the pre-funded warrants pursuant to the underwriting agreement described in the Preliminary Prospectus Supplement on terms generally consistent with those applicable to the shares of common stock being sold in the offering. The per share underwriting discounts and commissions for the pre-funded warrants will be equal to the per share underwriting discounts and commissions on the shares of common stock sold in the offering.

MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES

Although it is not entirely free from doubt, a pre-funded warrant should be treated as a share of our common stock for U.S. federal income tax purposes and a holder of pre-funded warrants should generally be taxed in the same manner as a holder of such common stock, as described below. Accordingly, no gain or loss should be recognized (other than with respect to cash paid in lieu of a fractional share) upon the exercise of a pre-funded warrant and, upon exercise, the holding period of a pre-funded warrant should carry over to the common stock received. Similarly, the tax basis of the pre-funded warrant should carry over to the share received upon exercise, increased by the exercise price per share. If a pre-funded warrant expires without being exercised, the holder thereof should recognize a capital loss in an amount equal to such holder's tax basis in the pre-funded warrant. This loss will be long-term capital loss if, at the time of the expiration, the holder's holding period in the pre-funded warrant is longer than one year. The deductibility of capital losses is subject to limitations.

Our characterization is not binding on the IRS, and the IRS may treat our pre-funded warrants as warrants to acquire our common stock. In that case, the amount and character of your gain with respect to an investment in our pre-funded warrants could be materially different than the discussion set forth in the section titled "Material U.S. Federal Income Tax Considerations For Non-U.S. Holders" in the accompanying base prospectus. Accordingly, each holder should consult his, her or its tax advisor regarding the risks associated with the acquisition of pre-funded warrants pursuant to this offering (including potential alternative characterizations).

GENERAL

Additional conforming changes are hereby made to the Preliminary Prospectus Supplement to reflect the changes described in this free writing prospectus. All terms of the Preliminary Prospectus Supplement applicable to our shares of our common stock will be applicable to the shares of common stock underlying the pre-funded warrants upon issuance.

Prime Medicine, Inc. has filed a registration statement (including a preliminary prospectus supplement dated February 14, 2024 and the accompanying base prospectus) with the Securities and Exchange Commission, or the SEC, for the offering to which this communication relates, declared effective by the SEC on November 13, 2023. Before you invest, you should read the preliminary prospectus supplement and the accompanying base prospectus and other documents Prime Medicine, Inc. has filed with the SEC for more complete information about Prime Medicine, Inc. and the offering. You may get these documents for free by visiting EDGAR on the SEC website at www.sec.gov. Alternatively, copies may be obtained by contacting: J.P. Morgan Securities LLC, Attention: Broadridge Financial Solutions, 1155 Long Island Avenue, Edgewood, New York 11717, by telephone at (866) 803-9204 or by email at prospectus-eq_fi@jpmchase.com; Jefferies LLC, Attention: Equity Syndicate Prospectus Department, 520 Madison Avenue, New York, New York 10022, by telephone at (877) 821-7388 or by email at Prospectus_Department@jefferies.com; Cowen and Company, LLC, 599 Lexington Avenue, New York, New York 10022, by telephone at (833) 297-2926 or by email at Prospectus_ECM@cowen.com; or BMO Capital Markets Corp., Attention: Equity Syndicate Department, 151 W 42nd Street, 32nd Floor, New York, New York 10036, by telephone at (800) 414-3627 or by email at bmoprospectus@bmo.com.