

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

POST-EFFECTIVE AMENDMENT NO. 1
TO

FORM S-3

REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

PRAXIS PRECISION MEDICINES, INC.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

47-5195942
(I.R.S. Employer
Identification Number)

**99 High Street, 30th Floor
Boston, MA 02110
(617) 300-8460**

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

**Marcio Souza
Chief Executive Officer
Praxis Precision Medicines, Inc.
99 High Street, 30th Floor
Boston, MA 02110
(617) 300-8460**

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

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(617) 300-8460**

APPROXIMATE DATE OF COMMENCEMENT OF PROPOSED SALE TO THE PUBLIC: From time to time after the effective date of this registration statement.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box.

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

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

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective on filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

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

Large accelerated filer
Non-accelerated filer

Accelerated filer
Smaller reporting company
Emerging growth company

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

EXPLANATORY NOTE

This Post-Effective Amendment No. 1 to the Registration Statement on Form S-3 (File No. 333-260726) (“Post-Effective Amendment No. 1”) of Praxis Precision Medicines, Inc. (the “Company”) is being filed because the Company expects that it will no longer be a “well-known seasoned issuer” (as such term is defined in Rule 405 of the Securities Act of 1933, as amended) when it files its Annual Report on Form 10-K for the fiscal year ended December 31, 2022. Accordingly, the Company is filing this Post-Effective Amendment No. 1 for the purpose of including disclosure required for a registrant other than a well-known seasoned issuer, identifying the securities being registered, registering a specific amount of securities and paying the associated filing fee.

This Post-Effective Amendment No. 1 contains:

- a base prospectus which covers the offering, issuance and sale by us of up to \$300,000,000 in the aggregate of the securities identified herein from time to time in one or more offerings; and
- a sales agreement prospectus supplement covering the offering, issuance and sale by us of up to a maximum aggregate offering price of \$95,573,843.36 of our common stock that may be issued and sold under an Open Market Sale AgreementSM, or the sales agreement, with Jefferies LLC acting as sales agent, or the ATM Program.

The base prospectus immediately follows this explanatory note. The specific terms of any securities to be offered pursuant to the base prospectus will be specified in a prospectus supplement to the base prospectus. The sales agreement prospectus supplement immediately follows the base prospectus. The \$95,573,843.36 of common stock that may be offered, issued and sold under the sales agreement prospectus is included in the \$300,000,000 of securities that may be offered, issued and sold by us under the base prospectus. As of the date of this Post-Effective Amendment No. 1, we have sold \$29,426,156.64 under the ATM Program. We are registering the offer and sale of the remaining \$95,573,843.36 that has not been sold under the ATM Program. Upon termination of the sales agreement with Jefferies LLC, any portion of the \$95,573,843.36 included in the sales agreement prospectus supplement that is not sold pursuant to the sales agreement will be available for sale in other offerings pursuant to the base prospectus and a corresponding prospectus supplement, and if none of such shares are sold, the full \$95,573,843.36 of securities may be sold in other offerings pursuant to the base prospectus and a corresponding prospectus supplement.

PROSPECTUS



PRAXIS PRECISION MEDICINES, INC.

\$300,000,000

Common Stock
Preferred Stock
Debt Securities
Warrants
Units

We may offer and sell up to \$300,000,000 in the aggregate of the securities identified above from time to time in one or more offerings. This prospectus provides you with a general description of the securities.

Each time we offer and sell securities, we will provide a supplement to this prospectus that contains specific information about the offering and the amounts, prices and terms of the securities. The supplement may also add, update or change information contained in this prospectus with respect to that offering. You should carefully read this prospectus and the applicable prospectus supplement before you invest in any of our securities.

We may offer and sell the securities described in this prospectus and any prospectus supplement to or through one or more underwriters, dealers and agents, or directly to purchasers, or through a combination of these methods. If any underwriters, dealers or agents are involved in the sale of any of the securities, their names and any applicable purchase price, fee, commission or discount arrangement between or among them will be set forth, or will be calculable from the information set forth, in the applicable prospectus supplement. See the sections of this prospectus entitled "About this Prospectus" and "Plan of Distribution" for more information. No securities may be sold without delivery of this prospectus and the applicable prospectus supplement describing the method and terms of the offering of such securities.

INVESTING IN OUR SECURITIES INVOLVES RISKS. SEE THE "RISK FACTORS" ON PAGE 7 OF THIS PROSPECTUS AND ANY SIMILAR SECTION CONTAINED IN THE APPLICABLE PROSPECTUS SUPPLEMENT CONCERNING FACTORS YOU SHOULD CONSIDER BEFORE INVESTING IN OUR SECURITIES.

Our common stock is listed on The Nasdaq Global Select Market under the symbol "PRAX." On February 3, 2023, the last reported sale price of our common stock on The Nasdaq Global Select Market was \$4.64 per share.

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 February 7, 2023.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the U.S. Securities and Exchange Commission, or the SEC, using a “shelf” registration process. By using a shelf registration statement, we may sell securities from time to time and in one or more offerings up to a total dollar amount of \$300,000,000 as described in this prospectus. Each time that we offer and sell securities, we will provide a prospectus supplement to this prospectus that contains specific information about the securities being offered and sold and the specific terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. The prospectus supplement or free writing prospectus may also add, update or change information contained in this prospectus with respect to that offering. If there is any inconsistency between the information in this prospectus and the applicable prospectus supplement or free writing prospectus, you should rely on the prospectus supplement or free writing prospectus, as applicable. Before purchasing any securities, you should carefully read both this prospectus and the applicable prospectus supplement (and any applicable free writing prospectuses), together with the additional information described under the heading “Where You Can Find More Information; Incorporation by Reference.”

We have not authorized anyone to provide you with any information or to make any representations other than those contained in this prospectus, any applicable prospectus supplement or any free writing prospectuses prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We will not make an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus and the applicable prospectus supplement to this prospectus is accurate only as of the date on its respective cover, that the information appearing in any applicable free writing prospectus is accurate only as of the date of that free writing prospectus, and that any information incorporated by reference is accurate only as of the date of the document incorporated by reference, unless we indicate otherwise. Our business, financial condition, results of operations and prospects may have changed since those dates. This prospectus incorporates by reference, and any prospectus supplement or free writing prospectus may contain and incorporate by reference, market data and industry statistics and forecasts that are based on independent industry publications and other publicly available information. Although we believe these sources are reliable, we do not guarantee the accuracy or completeness of this information and we have not independently verified this information. In addition, the market and industry data and forecasts that may be included or incorporated by reference in this prospectus, any prospectus supplement or any applicable free writing prospectus may involve estimates, assumptions and other risks and uncertainties and are subject to change based on various factors, including those discussed under the heading “Risk Factors” contained in this prospectus, the applicable prospectus supplement and any applicable free writing prospectus, and under similar headings in other documents that are incorporated by reference into this prospectus. Accordingly, investors should not place undue reliance on this information.

When we refer to “Praxis,” “we,” “our,” “us” and the “Company” in this prospectus, we mean Praxis Precision Medicines, Inc. and its consolidated subsidiaries, unless otherwise specified. When we refer to “you,” we mean the potential holders of the applicable series of securities.

We have proprietary rights to trademarks, trade names and service marks appearing in this prospectus and the documents incorporated by reference herein that are important to our business. Solely for convenience, the trademarks, trade names and service marks may appear in this prospectus and the documents incorporated by reference herein without the ® and ™ symbols, but any such references are not intended to indicate, in any way, that we forgo or will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensors to these trademarks, trade names and service marks. All trademarks, trade names and service marks appearing in this prospectus and the documents incorporated by reference herein are the property of their respective owners. We do not intend our use or display of other parties’ trademarks, trade names or service marks to imply, and such use or display should not be construed to imply, a relationship with, or endorsement or sponsorship of us by, these other parties.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, any applicable prospectus supplement, any related free writing prospectus and the documents that we incorporate by reference herein or therein contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. These statements are often, but are not always, made through the use of words or phrases such as “may,” “will,” “could,” “should,” “expects,” “intends,” “plans,” “anticipates,” “believes,” “estimates,” “predicts,” “projects,” “potential,” “continue,” and similar expressions, or the negative of these terms, or similar expressions. Accordingly, these statements involve estimates, assumptions, risks and uncertainties which could cause actual results to differ materially from those expressed in them. Any forward-looking statements are qualified in their entirety by reference to the factors discussed throughout this prospectus, and in particular those factors referenced in the section “Risk Factors.”

This prospectus contains forward-looking statements that are based on our management’s belief and assumptions and on information currently available to our management. These statements relate to future events or our future financial performance, and 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 these forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

- the success, cost and timing of our product candidate development activities and clinical trials;
- our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidates;
- the ability to license additional intellectual property relating to our product candidates from third parties and to comply with our existing license agreements and collaboration agreements;
- the ability and willingness of our third-party research institution collaborators to continue research and development activities relating to our product candidates;
- our ability to commercialize our product candidates, if approved, in light of the intellectual property rights of others;
- our ability to obtain funding for our operations, including funding necessary to complete further development and, if approved, commercialization of our product candidates;
- the commercialization of our product candidates, if approved;
- our plans to research, develop and, if approved, commercialize our product candidates;
- future agreements with third parties in connection with the commercialization of our product candidates, if approved, and any other approved product;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- the rate and degree of market acceptance of our product candidates, if approved;
- the pricing and reimbursement of our product candidates, if approved;
- regulatory developments in the United States and foreign countries;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- the success of competing therapies that are or may become available;
- our ability to attract and retain key scientific or management personnel; and
- the accuracy of our estimates regarding expenses, future revenue, capital requirements and needs for additional financing.

These forward-looking statements are neither promises nor guarantees of future performance due to a variety of risks and uncertainties, many of which are beyond our control, which could cause actual results to differ materially from those indicated by these forward-looking statements, including, without limitation 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, 2021 and our most recent Quarterly Reports on Form 10-Q for the quarters ended March 31, 2022, June 30, 2022 and September 30, 2022, our Current Reports on Form 8-K, and the section of any accompanying prospectus supplement entitled “Risk Factors.”

The forward-looking statements in this prospectus and the documents incorporated by reference represent our views as of their respective dates. 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 assume no obligation to update or revise any forward-looking statements 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 dates on which they were made.

This prospectus and the documents incorporated by reference also contain estimates, projections and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. 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 reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data 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.

WHERE YOU CAN FIND MORE INFORMATION; INCORPORATION BY REFERENCE

Available Information

We file reports, proxy statements and other information with the SEC. The SEC maintains a website that contains reports, proxy and information statements and other information about issuers, such as us, who file electronically with the SEC. The address of that website is <http://www.sec.gov>.

Our website address is <http://www.praxismedicines.com>. The information on our website, however, is not, and should not be deemed to be, a part of this prospectus.

This prospectus and any prospectus supplement are part of a registration statement that we filed with the SEC and do not contain all of the information in the registration statement. The full registration statement may be obtained from the SEC or us, as provided below. Forms of the indenture and other documents establishing the terms of the offered securities are or may be filed as exhibits to the registration statement or documents incorporated by reference in the registration statement. Statements in this prospectus or any prospectus supplement about these documents 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 by Reference

The SEC's rules allow us to "incorporate by reference" information into this prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus, and subsequent information that we file with the SEC will automatically update and supersede that information. Any statement contained in this prospectus or a previously filed document incorporated by reference will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or a subsequently filed document incorporated by reference modifies or replaces that statement.

This prospectus and any accompanying prospectus supplement incorporate by reference the documents set forth below that have previously been filed with the SEC:

- [Our Annual Report on Form 10-K for the year ended December 31, 2021, filed with the SEC on February 28, 2022.](#)
- [The information specifically incorporated by reference into our Annual Report on Form 10-K from our Definitive Proxy Statement on Schedule 14A, filed with the SEC on April 14, 2022.](#)
- Our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2022, June 30, 2022 and September 30, 2022, filed with the SEC on [May 9, 2022](#), [August 8, 2022](#) and [November 9, 2022](#), respectively.
- Our Current Reports on Form 8-K and Amended Current Reports on Form 8-K/A filed with the SEC on [January 7, 2022](#), [January 10, 2022](#) (Item 8.01 only), [April 29, 2022](#), [May 9, 2022](#) (Item 8.01 only), [May 23, 2022](#), [June 1, 2022](#), [June 6, 2022](#), [July 11, 2022](#), [July 26, 2022](#), [August 8, 2022](#) (Item 8.01 only), [August 12, 2022](#), [September 7, 2022](#) and [November 28, 2022](#) (Item 8.01 only).
- [The description of our Common Stock contained in the our Registration Statement on Form 8-A filed with the SEC on October 14, 2020 and any amendment or report filed with the SEC for the purpose of updating the description.](#)

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, which we refer to as the "Exchange Act" in this prospectus, prior to the termination of this offering but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus and deemed to be part of this prospectus from the date of the filing of such reports and documents.

You may request a free copy of any of the documents incorporated by reference in this prospectus by writing or telephoning us at the following address:

Praxis Precision Medicines, Inc.
99 High Street, 30th Floor
Boston, MA 02110
(617) 300-8460

Exhibits to the filings will not be sent, however, unless those exhibits have specifically been incorporated by reference in this prospectus or any accompanying prospectus supplement.

THE COMPANY

We are a clinical-stage biopharmaceutical company translating insights from genetic epilepsies into the development of therapies for central nervous system, or CNS, disorders characterized by neuronal excitation-inhibition imbalance. Normal brain function requires a delicate balance of excitation and inhibition in neuronal circuits, which, when dysregulated, can lead to abnormal function and both rare and more prevalent neurological disorders. We are applying genetic insights to the discovery and development of therapies for neurological disorders through two proprietary platforms, using our understanding of shared biological targets and circuits in the brain. Each platform currently has multiple programs, with significant potential for additional program and indication expansion:

- **Cerebrum™**, our small molecule platform, utilizes deep understanding of neuronal excitability and neuronal networks and applies a series of computational and experimental tools to develop orally available precision therapies
- **Solidus™**, our antisense oligonucleotide, or ASO, platform, is an efficient, targeted precision medicine discovery and development engine anchored on a proprietary, computational methodology

Our platforms utilize a deliberate, pragmatic and patient-guided approach, leveraging a suite of translational tools, including novel transgenic and predictive translational animal models and electrophysiology markers, to enable an efficient path to proof-of-concept in patients. Through this approach, we have established a diversified, multimodal CNS portfolio with four clinical-stage product candidates across movement disorders and epilepsy.

Corporate Information

We were incorporated under the laws of the State of Delaware on September 22, 2015. Our principal executive office is located at 99 High Street, 30th Floor, Boston, MA 02110, and our telephone number is (617) 300-8460. Our website address is www.praxismedicines.com. We do not incorporate the information on or accessible through our website into this prospectus supplement, and you should not consider any information on, or that can be accessed through, our website as part of this prospectus supplement.

RISK FACTORS

Investment in any securities offered pursuant to this prospectus and the applicable prospectus supplement involves risks. Before deciding whether to invest in our securities, you should carefully consider the risk factors incorporated by reference to our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q or Current Reports on Form 8-K, and all other information contained or incorporated by reference into this prospectus, as updated by our subsequent filings under the Exchange Act, and the risk factors and other information contained in the applicable prospectus supplement and any applicable free writing prospectus. The occurrence of any of these risks might cause you to lose all or part of your investment in the offered securities. There may be other unknown or unpredictable economic, business, competitive, regulatory or other factors that could have material adverse effects on our future results. Past financial performance may not be a reliable indicator of future performance, and historical trends should not be used to anticipate results or trends in future periods. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our securities to decline, resulting in a loss of all or part of your investment. Please also carefully read the section entitled “Special Note Regarding Forward-Looking Statements” included in our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q or Current Reports on Form 8-K.

USE OF PROCEEDS

We intend to use the net proceeds from the sale of the securities as set forth in the applicable prospectus supplement.

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock is not complete and may not contain all the information you should consider before investing in our capital stock. This description is summarized from, and qualified in its entirety by reference to, our certificate of incorporation, which has been publicly filed with the SEC. See “Where You Can Find More Information; Incorporation by Reference.”

Our authorized capital stock consists of:

- 150,000,000 shares of common stock, \$0.0001 par value; and
- 10,000,000 shares of preferred stock, \$0.0001 par value.

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 dividends declared by our board of directors out of funds legally available for that purpose. 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 pro rata in the distribution of our assets remaining after payment of all debts and other liabilities.

Preferred Stock

Our board of directors or any authorized committee thereof is authorized, 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.

Registration Rights

Pursuant to the terms of our Fourth Amended and Restated Investors’ Rights Agreement, dated as of July 24, 2020, as amended, or the Investors’ Rights Agreement, certain of our stockholders are entitled to rights with respect to the registration of their shares (which we refer to herein as “registrable securities”) under the Securities Act, including demand registration rights and piggyback registration rights.

Form S-1 Registration Rights

Under the terms of the Investors’ Rights Agreement, we are required, upon the request of holders holding at least a majority of the registrable securities then outstanding, to file a registration statement on Form S-1 registering the resale of such holders’ registrable securities and the registrable securities of such other holders who elect to have their shares registered; provided that the anticipated aggregate offering price, net of related fees and expenses, of the registrable securities registered on such registration statement would equal at least \$10 million. We are required to effect only two registrations pursuant to this provision of the Investors’ Rights Agreement. If the holders requesting registration intend to distribute their shares by means of an underwriting, the managing underwriter of such offering will have the right to limit the numbers of shares to be underwritten for reasons related to the marketing of the shares.

Form S-3 Registration Rights

Pursuant to the Investors’ Rights Agreement, if we are eligible to file a registration statement on Form S-3, we are required, upon the request of holders holding at least a majority of the registrable

securities then outstanding, to file a registration restatement on Form S-3 registering the resale of such holders' registrable securities and the registrable securities of such other holders who elect to have their shares registered; provided that the anticipated aggregate offering price, net of related fees and expenses, of the registrable securities registered on such registration statement would equal at least \$3 million. We are required to effect only two registrations in any twelve-month period pursuant to this provision of the Investors' Rights Agreement. If the holders requesting registration intend to distribute their shares by means of an underwriting, the managing underwriter of such offering will have the right to limit the numbers of shares to be underwritten for reasons related to the marketing of the shares.

Piggyback Registration Rights

Subject to certain exceptions, if we register any of our securities either for our own account or for the account of security holders other than the holders party to the Investors' Rights Agreements, the holders of shares of registrable securities are entitled to include their shares in the registration. If our proposed registration involves an underwriting, the managing underwriter of such offering will have the right to limit the number of shares to be underwritten for reasons related to the marketing of the shares.

Indemnification

The 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 Investors' Rights Agreement will terminate on the earliest to occur of: (i) the fifth anniversary of the completion of our initial public offering and (ii) as to each holder of registrable securities, such time as either Rule 144 as promulgated under the Securities Act or another similar exemption under the Securities Act is available for the sale of all of such holder's shares without limitation during a three-month period without registration or such holder no longer holds any registrable securities.

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

Our certificate of incorporation and bylaws include a number of provisions that may 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.

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.

Exclusive Jurisdiction for Certain Actions

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 will be the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of or based on a fiduciary duty owed by any current or former director, officer or other employee or stockholder to us or our stockholders, (iii) any action asserting a claim against us or any current or former director, officer or other employee or stockholder arising pursuant to any provision of the DGCL, our certificate of incorporation or our bylaws or as to which the DGCL confers jurisdiction on the Court of Chancery of the State of Delaware, or (iv) any action asserting a claim governed by the internal affairs doctrine, in each case subject to said Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein; provided that, the provisions of this sentence do not apply to suits brought to enforce any liability or duty created by the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, or any other claim for which the federal courts have exclusive jurisdiction; and provided further that, if and only if the Court of Chancery of the State of Delaware dismisses any such action for lack of subject matter jurisdiction, such action may be brought in another state or federal court sitting in the State of Delaware. Unless the Corporation consents in writing to the selection of an alternative forum, the federal district courts of the United States of America shall, to the fullest extent permitted by law, be the sole and exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act of 1933, as amended. Any person or entity purchasing or otherwise acquiring any interest in shares of capital stock of the Corporation shall be deemed to have notice of and consented to these exclusive jurisdiction provisions.

Section 203 of the Delaware General Corporation Law

We are subject to Section 203 of the General Corporation Law of the State of Delaware, which prohibits persons deemed to be “interested stockholders” from engaging in a “business combination” with a publicly held Delaware corporation for three years following the date these persons become interested stockholders unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies. Generally, an “interested stockholder” is a person who, together with affiliates and associates, owns, or within three years prior to the determination of interested stockholder status did own, 15% or more of a corporation’s voting stock. Generally, a “business combination” includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. The existence of this provision may have an anti-takeover effect with respect to transactions not approved in advance by the board of directors.

Certificate of Incorporation and Bylaws

Provisions of our certificate of incorporation and our bylaws may delay or discourage transactions involving an actual or potential change in our control or change in our management, including transactions in which stockholders might otherwise receive a premium for their shares or transactions that our stockholders might otherwise deem to be in their best interests. Therefore, these provisions could adversely affect the price of our common stock. Among other things, our certificate of incorporation and bylaws:

- permit our board of directors or any authorized committee thereof to issue up to 10,000,000 shares of preferred stock, with any rights, preferences and privileges as they may designate;
- provide that the authorized number of directors may be changed only by resolution adopted by the board of directors;
- provide that the board of directors or any individual director may only be removed with cause and the affirmative vote of the holders of at least two thirds of the outstanding shares of capital stock then entitled vote at an election of directors;
- provide that all vacancies, including newly created directorships, may, subject to the rights of holders of preferred stock as designated from time to time, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum;
- divide our board of directors into three classes;

- require that any action to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and not be taken by written consent;
- provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide notice in writing in a timely manner and also specify requirements as to the form and content of a stockholder's notice;
- do not provide for cumulative voting rights (therefore allowing the holders of a majority of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election, if they should so choose);
- provide that special meetings of our stockholders may be called only by our board of directors acting pursuant to a resolution approved by the affirmative vote of a majority of the directors then in office; and
- provide that the Court of Chancery of the State of Delaware will be the sole and exclusive forum for state law claims, as described above.

The amendment of any of these provisions included in our certificate of incorporation, with the exception of the ability of our board of directors to issue shares of preferred stock and designate any rights, preferences and privileges thereto, the removal of directors by our stockholders, the filling of vacancies by our board of directors, and cumulative voting rights, would require the affirmative vote of two thirds of the outstanding shares of capital stock entitled to vote on such amendment and the affirmative vote of two thirds of the outstanding shares of each class entitled to vote on such amendment as a class.

The amendment of any of these provisions included in our bylaws, with the exception of the exclusive forum provision, would require the affirmative vote of two thirds of the outstanding shares of capital stock entitled to vote on such amendment, and the affirmative vote of not less than two thirds of the outstanding shares of each class entitled to vote on such amendment as a class; provided, however, that if our Board of Directors recommends that stockholders approve such amendment, such amendment shall only require the affirmative vote of a majority of the outstanding shares entitled to vote on such amendment, voting together as a single class.

Transfer agent and registrar

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

DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplement or free writing prospectus, summarizes certain general terms and provisions of the debt securities that we may offer under this prospectus. When we offer to sell a particular series of debt securities, we will describe the specific terms of the series in a supplement to this prospectus. We will also indicate in the supplement to what extent the general terms and provisions described in this prospectus apply to a particular series of debt securities.

We may issue debt securities either separately, or together with, or upon the conversion or exercise of or in exchange for, other securities described in this prospectus. Debt securities may be our senior, senior subordinated or subordinated obligations and, unless otherwise specified in a supplement to this prospectus, the debt securities will be our direct, unsecured obligations and may be issued in one or more series.

The debt securities will be issued under an indenture between us and a trustee to be named in the applicable indenture, as trustee. We have summarized select portions of the indenture below. The summary is not complete. The form of the indenture has been filed as an exhibit to the registration statement and you should read the indenture for provisions that may be important to you. In the summary below, we have included references to the section numbers of the indenture so that you can easily locate these provisions. Capitalized terms used in the summary and not defined herein have the meanings specified in the indenture.

As used in this section only, “Praxis,” “we,” “our” or “us” refer to Praxis Precision Medicines, Inc. excluding our subsidiaries, unless expressly stated or the context otherwise requires.

General

The terms of each series of debt securities will be established by or pursuant to a resolution of our board of directors and set forth or determined in the manner provided in a resolution of our board of directors, in an officer’s certificate or by a supplemental indenture. (Section 2.2) The particular terms of each series of debt securities will be described in a prospectus supplement relating to such series (including any pricing supplement or term sheet).

We can issue an unlimited amount of debt securities under the indenture that may be in one or more series with the same or various maturities, at par, at a premium, or at a discount. (Section 2.1) We will set forth in a prospectus supplement (including any pricing supplement or term sheet) relating to any series of debt securities being offered, the aggregate principal amount and the following terms of the debt securities, if applicable:

- the title and ranking of the debt securities (including the terms of any subordination provisions);
- the price or prices (expressed as a percentage of the principal amount) at which we will sell the debt securities;
- any limit on the aggregate principal amount of the debt securities;
- the date or dates on which the principal of the securities of the series is payable;
- the rate or rates (which may be fixed or variable) per annum or the method used to determine the rate or rates (including any commodity, commodity index, stock exchange index or financial index) at which the debt securities will bear interest, the date or dates from which interest will accrue, the date or dates on which interest will commence and be payable and any regular record date for the interest payable on any interest payment date;
- the place or places where principal of, and interest, if any, on the debt securities will be payable (and the method of such payment), where the securities of such series may be surrendered for registration of transfer or exchange, and where notices and demands to us in respect of the debt securities may be delivered;
- the period or periods within which, the price or prices at which and the terms and conditions upon which we may redeem the debt securities;

- any obligation we have to redeem or purchase the debt securities pursuant to any sinking fund or analogous provisions or at the option of a holder of debt securities and the period or periods within which, the price or prices at which and in the terms and conditions upon which securities of the series shall be redeemed or purchased, in whole or in part, pursuant to such obligation;
- the dates on which and the price or prices at which we will repurchase debt securities at the option of the holders of debt securities and other detailed terms and provisions of these repurchase obligations;
- the denominations in which the debt securities will be issued, if other than denominations of \$1,000 and any integral multiple thereof;
- whether the debt securities will be issued in the form of certificated debt securities or global debt securities;
- the portion of principal amount of the debt securities payable upon declaration of acceleration of the maturity date, if other than the principal amount;
- the currency of denomination of the debt securities, which may be United States Dollars or any foreign currency, and if such currency of denomination is a composite currency, the agency or organization, if any, responsible for overseeing such composite currency;
- the designation of the currency, currencies or currency units in which payment of principal of, premium and interest on the debt securities will be made;
- if payments of principal of, premium or interest on the debt securities will be made in one or more currencies or currency units other than that or those in which the debt securities are denominated, the manner in which the exchange rate with respect to these payments will be determined;
- the manner in which the amounts of payment of principal of, premium, if any, or interest on the debt securities will be determined, if these amounts may be determined by reference to an index based on a currency or currencies or by reference to a commodity, commodity index, stock exchange index or financial index;
- any provisions relating to any security provided for the debt securities;
- any addition to, deletion of or change in the Events of Default described in this prospectus or in the indenture with respect to the debt securities and any change in the acceleration provisions described in this prospectus or in the indenture with respect to the debt securities;
- any addition to, deletion of or change in the covenants described in this prospectus or in the indenture with respect to the debt securities;
- any depositaries, interest rate calculation agents, exchange rate calculation agents or other agents with respect to the debt securities;
- the provisions, if any, relating to conversion or exchange of any debt securities of such series, including if applicable, the conversion or exchange price and period, provisions as to whether conversion or exchange will be mandatory, the events requiring an adjustment of the conversion or exchange price and provisions affecting conversion or exchange;
- any other terms of the debt securities, which may supplement, modify or delete any provision of the indenture as it applies to that series, including any terms that may be required under applicable law or regulations or advisable in connection with the marketing of the securities; and
- whether any of our direct or indirect subsidiaries will guarantee the debt securities of that series, including the terms of subordination, if any, of such guarantees. (Section 2.2)

We may issue debt securities that provide for an amount less than their stated principal amount to be due and payable upon declaration of acceleration of their maturity pursuant to the terms of the indenture. We will provide you with information on the federal income tax considerations and other special considerations applicable to any of these debt securities in the applicable prospectus supplement.

If we denominate the purchase price of any of the debt securities in a foreign currency or currencies or a foreign currency unit or units, or if the principal of and any premium and interest on any series of debt

securities is payable in a foreign currency or currencies or a foreign currency unit or units, we will provide you with information on the restrictions, elections, general tax considerations, specific terms and other information with respect to that issue of debt securities and such foreign currency or currencies or foreign currency unit or units in the applicable prospectus supplement.

Transfer and Exchange

Each debt security will be represented by either one or more global securities registered in the name of The Depository Trust Company, or the Depository, or a nominee of the Depository (we will refer to any debt security represented by a global debt security as a “book-entry debt security”), or a certificate issued in definitive registered form (we will refer to any debt security represented by a certificated security as a “certificated debt security”) as set forth in the applicable prospectus supplement. Except as set forth under the heading “Global Debt Securities and Book-Entry System” below, book-entry debt securities will not be issuable in certificated form.

Certificated Debt Securities. You may transfer or exchange certificated debt securities at any office we maintain for this purpose in accordance with the terms of the indenture. (Section 2.4) No service charge will be made for any transfer or exchange of certificated debt securities, but we may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection with a transfer or exchange. (Section 2.7)

You may effect the transfer of certificated debt securities and the right to receive the principal of, premium and interest on certificated debt securities only by surrendering the certificate representing those certificated debt securities and either reissuance by us or the trustee of the certificate to the new holder or the issuance by us or the trustee of a new certificate to the new holder.

Global Debt Securities and Book-Entry System. Each global debt security representing book-entry debt securities will be deposited with, or on behalf of, the Depository, and registered in the name of the Depository or a nominee of the Depository. Please see “Global Securities.”

Covenants

We will set forth in the applicable prospectus supplement any restrictive covenants applicable to any issue of debt securities. (Article IV)

No Protection in the Event of a Change of Control

Unless we state otherwise in the applicable prospectus supplement, the debt securities will not contain any provisions which may afford holders of the debt securities protection in the event we have a change in control or in the event of a highly leveraged transaction (whether or not such transaction results in a change in control) which could adversely affect holders of debt securities.

Consolidation, Merger and Sale of Assets

We may not consolidate with or merge with or into, or convey, transfer or lease all or substantially all of our properties and assets to any person (a “successor person”) unless:

- we are the surviving entity or the successor person (if other than Praxis) is a corporation, partnership, trust or other entity organized and validly existing under the laws and expressly assumes our obligations on the debt securities and under the indenture; and
- immediately after giving effect to the transaction, no Default or Event of Default, shall have occurred and be continuing.

Notwithstanding the above, any of our subsidiaries may consolidate with, merge into or transfer all or part of its properties to us. (Section 5.1)

Events of Default

“Event of Default” means with respect to any series of debt securities, any of the following:

- default in the payment of any interest upon any debt security of that series when it becomes due and payable, and continuance of such default for a period of 30 days (unless the entire amount of the payment is deposited by us with the trustee or with a paying agent prior to the expiration of the 30-day period);
- default in the payment of principal of any security of that series at its maturity;
- default in the performance or breach of any other covenant or warranty by us in the indenture (other than a covenant or warranty that has been included in the indenture solely for the benefit of a series of debt securities other than that series), which default continues uncured for a period of 60 days after we receive written notice from the trustee or Praxis and the trustee receive written notice from the holders of not less than 25% in principal amount of the outstanding debt securities of that series as provided in the indenture;
- certain voluntary or involuntary events of bankruptcy, insolvency or reorganization of Praxis;
- any other Event of Default provided with respect to debt securities of that series that is described in the applicable prospectus supplement. (Section 6.1)

No Event of Default with respect to a particular series of debt securities (except as to certain events of bankruptcy, insolvency or reorganization) necessarily constitutes an Event of Default with respect to any other series of debt securities. (Section 6.1) The occurrence of certain Events of Default or an acceleration under the indenture may constitute an event of default under certain indebtedness of ours or our subsidiaries outstanding from time to time.

We will provide the trustee written notice of any Default or Event of Default within 30 days of becoming aware of the occurrence of such Default or Event of Default, which notice will describe in reasonable detail the status of such Default or Event of Default and what action we are taking or propose to take in respect thereof. (Section 6.1)

If an Event of Default with respect to debt securities of any series at the time outstanding occurs and is continuing, then the trustee or the holders of not less than 25% in principal amount of the outstanding debt securities of that series may, by a notice in writing to us (and to the trustee if given by the holders), declare to be due and payable immediately the principal of (or, if the debt securities of that series are discount securities, that portion of the principal amount as may be specified in the terms of that series) and accrued and unpaid interest, if any, on all debt securities of that series. In the case of an Event of Default resulting from certain events of bankruptcy, insolvency or reorganization, the principal (or such specified amount) of and accrued and unpaid interest, if any, on all outstanding debt securities will become and be immediately due and payable without any declaration or other act on the part of the trustee or any holder of outstanding debt securities. At any time after a declaration of acceleration with respect to debt securities of any series has been made, but before a judgment or decree for payment of the money due has been obtained by the trustee, the holders of a majority in principal amount of the outstanding debt securities of that series may rescind and annul the acceleration if all Events of Default, other than the non-payment of accelerated principal and interest, if any, with respect to debt securities of that series, have been cured or waived as provided in the indenture. (Section 6.2) We refer you to the prospectus supplement relating to any series of debt securities that are discount securities for the particular provisions relating to acceleration of a portion of the principal amount of such discount securities upon the occurrence of an Event of Default.

The indenture provides that the trustee may refuse to perform any duty or exercise any of its rights or powers under the indenture unless the trustee receives indemnity satisfactory to it against any cost, liability or expense which might be incurred by it in performing such duty or exercising such right or power. (Section 7.1(e)) Subject to certain rights of the trustee, 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. (Section 6.12)

No holder of any debt security of any series will have any right to institute any proceeding, judicial or otherwise, with respect to the indenture or for the appointment of a receiver or trustee, or for any remedy under the indenture, unless:

- that holder has previously given to the trustee written notice of a continuing Event of Default with respect to debt securities of that series; and
- the holders of not less than 25% in principal amount of the outstanding debt securities of that series have made written request, and offered indemnity or security satisfactory to the trustee, to the trustee to institute the proceeding as trustee, and the trustee has not received from the holders of not less than a majority in principal amount of the outstanding debt securities of that series a direction inconsistent with that request and has failed to institute the proceeding within 60 days. (Section 6.7)

Notwithstanding any other provision in the indenture, the holder of any debt security will have an absolute and unconditional right to receive payment of the principal of, premium and any interest on that debt security on or after the due dates expressed in that debt security and to institute suit for the enforcement of payment. (Section 6.8)

The indenture requires us, within 120 days after the end of our fiscal year, to furnish to the trustee a statement as to compliance with the indenture. (Section 4.3) If a Default or Event of Default occurs and is continuing with respect to the securities of any series and if it is known to a responsible officer of the trustee, the trustee shall mail to each Securityholder of the securities of that series notice of a Default or Event of Default within 90 days after it occurs or, if later, after a responsible officer of the trustee has knowledge of such Default or Event of Default. The indenture provides that the trustee may withhold notice to the holders of debt securities of any series of any Default or Event of Default (except in payment on any debt securities of that series) with respect to debt securities of that series if the trustee determines in good faith that withholding notice is in the interest of the holders of those debt securities. (Section 7.5)

Modification and Waiver

We and the trustee may modify, amend or supplement the indenture or the debt securities of any series without the consent of any holder of any debt security:

- to cure any ambiguity, defect or inconsistency;
- to comply with covenants in the indenture described above under the heading “Consolidation, Merger and Sale of Assets”;
- to provide for uncertificated securities in addition to or in place of certificated securities;
- to add guarantees with respect to debt securities of any series or secure debt securities of any series;
- to surrender any of our rights or powers under the indenture;
- to add covenants or events of default for the benefit of the holders of debt securities of any series;
- to comply with the applicable procedures of the applicable depository;
- to make any change that does not adversely affect the rights of any holder of debt securities;
- to provide for the issuance of and establish the form and terms and conditions of debt securities of any series as permitted by the indenture;
- to effect the appointment of a successor trustee with respect to the debt securities of any series and to add to or change any of the provisions of the indenture to provide for or facilitate administration by more than one trustee; or
- to comply with requirements of the SEC in order to effect or maintain the qualification of the indenture under the Trust Indenture Act. (Section 9.1)

We may also modify and amend the indenture with the consent of the holders of at least a majority in principal amount of the outstanding debt securities of each series affected by the modifications or amendments. We may not make any modification or amendment without the consent of the holders of each affected debt security then outstanding if that amendment will:

- reduce the amount of debt securities whose holders must consent to an amendment, supplement or waiver;

- reduce the rate of or extend the time for payment of interest (including default interest) on any debt security;
- reduce the principal of or premium on or change the fixed maturity of any debt security or reduce the amount of, or postpone the date fixed for, the payment of any sinking fund or analogous obligation with respect to any series of debt securities;
- reduce the principal amount of discount securities payable upon acceleration of maturity;
- waive a default in the payment of the principal of, premium or interest on any debt security (except a rescission of acceleration of the debt securities of any series by the holders of at least a majority in aggregate principal amount of the then outstanding debt securities of that series and a waiver of the payment default that resulted from such acceleration);
- make the principal of or premium or interest on any debt security payable in currency other than that stated in the debt security;
- make any change to certain provisions of the indenture relating to, among other things, the right of holders of debt securities to receive payment of the principal of, premium and interest on those debt securities and to institute suit for the enforcement of any such payment and to waivers or amendments; or
- waive a redemption payment with respect to any debt security. (Section 9.3)

Except for certain specified provisions, the holders of at least a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all debt securities of that series waive our compliance with provisions of the indenture. (Section 9.2) The holders of a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all the debt securities of such series waive any past default under the indenture with respect to that series and its consequences, except a default in the payment of the principal of, premium or any interest on any debt security of that series; provided, however, that the holders of a majority in principal amount of the outstanding debt securities of any series may rescind an acceleration and its consequences, including any related payment default that resulted from the acceleration. (Section 6.13)

Defeasance of Debt Securities and Certain Covenants in Certain Circumstances

Legal Defeasance. The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, we may be discharged from any and all obligations in respect of the debt securities of any series (subject to certain exceptions). We will be so discharged upon the irrevocable deposit with the trustee, in trust, of money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. Dollars, government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money or U.S. government obligations in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal, premium and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities.

This discharge may occur only if, among other things, we have delivered to the trustee an opinion of counsel stating that we have received from, or there has been published by, the United States Internal Revenue Service a ruling or, since the date of execution of the indenture, there has been a change in the applicable United States federal income tax law, in either case to the effect that, and based thereon such opinion shall confirm that, the holders of the debt securities of that series will not recognize income, gain or loss for United States federal income tax purposes as a result of the deposit, defeasance and discharge and will be subject to United States federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit, defeasance and discharge had not occurred. (Section 8.3)

Defeasance of Certain Covenants. The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, upon compliance with certain conditions:

- we may omit to comply with the covenant described under the heading “Consolidation, Merger and Sale of Assets” and certain other covenants set forth in the indenture, as well as any additional covenants which may be set forth in the applicable prospectus supplement; and
- any omission to comply with those covenants will not constitute a Default or an Event of Default with respect to the debt securities of that series (“covenant defeasance”).

The conditions include:

- depositing with the trustee money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. Dollars, government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal of, premium and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities; and
- delivering to the trustee an opinion of counsel to the effect that the holders of the debt securities of that series will not recognize income, gain or loss for United States federal income tax purposes as a result of the deposit and related covenant defeasance and will be subject to United States federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit and related covenant defeasance had not occurred. (Section 8.4)

No Personal Liability of Directors, Officers, Employees or Securityholders

None of our past, present or future directors, officers, employees or securityholders, as such, will have any liability for any of our obligations under the debt securities or the indenture or for any claim based on, or in respect or by reason of, such obligations or their creation. By accepting a debt security, each holder waives and releases all such liability. This waiver and release is part of the consideration for the issue of the debt securities. However, this waiver and release may not be effective to waive liabilities under U.S. federal securities laws, and it is the view of the SEC that such a waiver is against public policy.

Governing Law

The indenture and the debt securities, including any claim or controversy arising out of or relating to the indenture or the securities, will be governed by the laws of the State of New York.

The indenture will provide that we, the trustee and the holders of the debt securities (by their acceptance of the debt securities) irrevocably waive, to the fullest extent permitted by applicable law, any and all right to trial by jury in any legal proceeding arising out of or relating to the indenture, the debt securities or the transactions contemplated thereby.

The indenture will provide that any legal suit, action or proceeding arising out of or based upon the indenture or the transactions contemplated thereby may be instituted in the federal courts of the United States of America located in the City of New York or the courts of the State of New York in each case located in the City of New York, and we, the trustee and the holder of the debt securities (by their acceptance of the debt securities) irrevocably submit to the non-exclusive jurisdiction of such courts in any such suit, action or proceeding. The indenture will further provide that service of any process, summons, notice or document by mail (to the extent allowed under any applicable statute or rule of court) to such party’s address set forth in the indenture will be effective service of process for any suit, action or other proceeding brought in any such court. The indenture will further provide that we, the trustee and the holders of the debt securities (by their acceptance of the debt securities) irrevocably and unconditionally waive any objection to the laying of venue of any suit, action or other proceeding in the courts specified above and irrevocably and unconditionally waive and agree not to plead or claim any such suit, action or other proceeding has been brought in an inconvenient forum. (Section 10.10)

DESCRIPTION OF WARRANTS

We may issue warrants for the purchase of shares of our common stock or preferred stock or of debt securities. We may issue warrants independently or together with other securities, and the warrants may be attached to or separate from any offered securities. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and the investors or a warrant agent. The following summary of material provisions of the warrants and warrant agreements are subject to, and qualified in their entirety by reference to, all the provisions of the warrant agreement and warrant certificate applicable to a particular series of warrants. The terms of any warrants offered under a prospectus supplement may differ from the terms described below. We urge you to read the applicable prospectus supplement and any related free writing prospectus, as well as the complete warrant agreements and warrant certificates that contain the terms of the warrants.

The particular terms of any issue of warrants will be described in the prospectus supplement relating to the issue. Those terms may include:

- the number of shares of common stock or preferred stock purchasable upon the exercise of warrants to purchase such shares and the price at which such number of shares may be purchased upon such exercise;
- the designation, stated value and terms (including, without limitation, liquidation, dividend, conversion and voting rights) of the series of preferred stock purchasable upon exercise of warrants to purchase preferred stock;
- the principal amount of debt securities that may be purchased upon exercise of a debt warrant and the exercise price for the warrants, which may be payable in cash, securities or other property;
- the date, if any, on and after which the warrants and the related debt securities, preferred stock or common stock will be separately transferable;
- the terms of any rights to redeem or call the warrants;
- the date on which the right to exercise the warrants will commence and the date on which the right will expire;
- United States Federal income tax consequences applicable to the warrants; and
- any additional terms of the warrants, including terms, procedures, and limitations relating to the exchange, exercise and settlement of the warrants.

Holders of equity warrants will not be entitled:

- to vote, consent or receive dividends;
- receive notice as shareholders with respect to any meeting of shareholders for the election of our directors or any other matter; or
- exercise any rights as shareholders of Praxis.

Each warrant will entitle its holder to purchase the principal amount of debt securities or the number of shares of preferred stock or common stock at the exercise price set forth in, or calculable as set forth in, the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to the specified time on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

A holder of warrant certificates may exchange them for new warrant certificates of different denominations, present them for registration of transfer and exercise them at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement. Until any warrants to purchase debt securities are exercised, the holder of the warrants will not have any rights of holders of the debt securities that can be purchased upon exercise, including any rights to receive payments of principal, premium or interest on the underlying debt securities or to enforce covenants in the applicable indenture. Until any warrants to purchase common stock or preferred stock are exercised, the holders of the warrants

will not have any rights of holders of the underlying common stock or preferred stock, including any rights to receive dividends or payments upon any liquidation, dissolution or winding up on the common stock or preferred stock, if any.

DESCRIPTION OF UNITS

We may issue units consisting of any combination of the other types of securities offered under this prospectus in one or more series. We may evidence each series of units by unit certificates that we will issue under a separate agreement. We may enter into unit agreements with a unit agent. Each unit agent will be a bank or trust company that we select. We will indicate the name and address of the unit agent in the applicable prospectus supplement relating to a particular series of units.

The following description, together with the additional information included in any applicable prospectus supplement, summarizes the general features of the units that we may offer under this prospectus. You should read any prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the series of units being offered, as well as the complete unit agreements that contain the terms of the units. Specific unit agreements will contain additional important terms and provisions and we will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from another report that we file with the SEC, the form of each unit agreement relating to units offered under this prospectus.

If we offer any units, certain terms of that series of units will be described in the applicable prospectus supplement, including, without limitation, the following, as applicable:

- the title of the series of units;
- identification and description of the separate constituent securities comprising the units;
- the price or prices at which the units will be issued;
- the date, if any, on and after which the constituent securities comprising the units will be separately transferable;
- a discussion of certain United States federal income tax considerations applicable to the units; and
- any other terms of the units and their constituent securities.

GLOBAL SECURITIES

Book-Entry, Delivery and Form

Unless we indicate differently in any applicable prospectus supplement or free writing prospectus, the securities initially will be issued in book-entry form and represented by one or more global notes or global securities, or, collectively, global securities. The global securities will be deposited with, or on behalf of, The Depository Trust Company, New York, New York, as depository, or DTC, and registered in the name of Cede & Co., the nominee of DTC. Unless and until it is exchanged for individual certificates evidencing securities under the limited circumstances described below, a global security may not be transferred except as a whole by the depository to its nominee or by the nominee to the depository, or by the depository or its nominee to a successor depository or to a nominee of the successor depository.

DTC has advised us that it is:

- a limited-purpose trust company organized under the New York Banking Law;
- a “banking organization” within the meaning of the New York Banking Law;
- a member of the Federal Reserve System;
- a “clearing corporation” within the meaning of the New York Uniform Commercial Code; and
- a “clearing agency” registered pursuant to the provisions of Section 17A of the Exchange Act.

DTC holds securities that its participants deposit with DTC. DTC also facilitates the settlement among its participants of securities transactions, such as transfers and pledges, in deposited securities through electronic computerized book-entry changes in participants’ accounts, thereby eliminating the need for physical movement of securities certificates. “Direct participants” in DTC include securities brokers and dealers, including underwriters, banks, trust companies, clearing corporations and other organizations. DTC is a wholly-owned subsidiary of The Depository Trust & Clearing Corporation, or DTCC. DTCC is the holding company for DTC, National Securities Clearing Corporation and Fixed Income Clearing Corporation, all of which are registered clearing agencies. DTCC is owned by the users of its regulated subsidiaries. Access to the DTC system is also available to others, which we sometimes refer to as indirect participants, that clear through or maintain a custodial relationship with a direct participant, either directly or indirectly. The rules applicable to DTC and its participants are on file with the SEC.

Purchases of securities under the DTC system must be made by or through direct participants, which will receive a credit for the securities on DTC’s records. The ownership interest of the actual purchaser of a security, which we sometimes refer to as a beneficial owner, is in turn recorded on the direct and indirect participants’ records. Beneficial owners of securities will not receive written confirmation from DTC of their purchases. However, beneficial owners are expected to receive written confirmations providing details of their transactions, as well as periodic statements of their holdings, from the direct or indirect participants through which they purchased securities. Transfers of ownership interests in global securities are to be accomplished by entries made on the books of participants acting on behalf of beneficial owners. Beneficial owners will not receive certificates representing their ownership interests in the global securities, except under the limited circumstances described below.

To facilitate subsequent transfers, all global securities deposited by direct participants with DTC will be registered in the name of DTC’s partnership nominee, Cede & Co., or such other name as may be requested by an authorized representative of DTC. The deposit of securities with DTC and their registration in the name of Cede & Co. or such other nominee will not change the beneficial ownership of the securities. DTC has no knowledge of the actual beneficial owners of the securities. DTC’s records reflect only the identity of the direct participants to whose accounts the securities are credited, which may or may not be the beneficial owners. The participants are responsible for keeping account of their holdings on behalf of their customers.

So long as the securities are in book-entry form, you will receive payments and may transfer securities only through the facilities of the depository and its direct and indirect participants. We will maintain an office or agency in the location specified in the prospectus supplement for the applicable securities, where notices and demands in respect of the securities and the indenture may be delivered to us and where certificated securities may be surrendered for payment, registration of transfer or exchange.

Conveyance of notices and other communications by DTC to direct participants, by direct participants to indirect participants and by direct participants and indirect participants to beneficial owners will be governed by arrangements among them, subject to any legal requirements in effect from time to time.

Redemption notices will be sent to DTC. If less than all of the securities of a particular series are being redeemed, DTC's practice is to determine by lot the amount of the interest of each direct participant in the securities of such series to be redeemed.

Neither DTC nor Cede & Co. (or such other DTC nominee) will consent or vote with respect to the securities. Under its usual procedures, DTC will mail an omnibus proxy to us as soon as possible after the record date. The omnibus proxy assigns the consenting or voting rights of Cede & Co. to those direct participants to whose accounts the securities of such series are credited on the record date, identified in a listing attached to the omnibus proxy.

So long as securities are in book-entry form, we will make payments on those securities to the depository or its nominee, as the registered owner of such securities, by wire transfer of immediately available funds. If securities are issued in definitive certificated form under the limited circumstances described below and unless if otherwise provided in the description of the applicable securities herein or in the applicable prospectus supplement, we will have the option of making payments by check mailed to the addresses of the persons entitled to payment or by wire transfer to bank accounts in the United States designated in writing to the applicable trustee or other designated party at least 15 days before the applicable payment date by the persons entitled to payment, unless a shorter period is satisfactory to the applicable trustee or other designated party.

Redemption proceeds, distributions and dividend payments on the securities will be made to Cede & Co., or such other nominee as may be requested by an authorized representative of DTC. DTC's practice is to credit direct participants' accounts upon DTC's receipt of funds and corresponding detail information from us on the payment date in accordance with their respective holdings shown on DTC records. Payments by participants to beneficial owners will be governed by standing instructions and customary practices, as is the case with securities held for the account of customers in bearer form or registered in "street name." Those payments will be the responsibility of participants and not of DTC or us, subject to any statutory or regulatory requirements in effect from time to time. Payment of redemption proceeds, distributions and dividend payments to Cede & Co., or such other nominee as may be requested by an authorized representative of DTC, is our responsibility, disbursement of payments to direct participants is the responsibility of DTC, and disbursement of payments to the beneficial owners is the responsibility of direct and indirect participants.

Except under the limited circumstances described below, purchasers of securities will not be entitled to have securities registered in their names and will not receive physical delivery of securities. Accordingly, each beneficial owner must rely on the procedures of DTC and its participants to exercise any rights under the securities and the indenture.

The laws of some jurisdictions may require that some purchasers of securities take physical delivery of securities in definitive form. Those laws may impair the ability to transfer or pledge beneficial interests in securities.

DTC may discontinue providing its services as securities depository with respect to the securities at any time by giving reasonable notice to us. Under such circumstances, in the event that a successor depository is not obtained, securities certificates are required to be printed and delivered.

As noted above, beneficial owners of a particular series of securities generally will not receive certificates representing their ownership interests in those securities. However, if:

- DTC notifies us that it is unwilling or unable to continue as a depository for the global security or securities representing such series of securities or if DTC ceases to be a clearing agency registered under the Exchange Act at a time when it is required to be registered and a successor depository is not appointed within 90 days of the notification to us or of our becoming aware of DTC's ceasing to be so registered, as the case may be;
- we determine, in our sole discretion, not to have such securities represented by one or more global securities; or

- an Event of Default has occurred and is continuing with respect to such series of securities,

we will prepare and deliver certificates for such securities in exchange for beneficial interests in the global securities. Any beneficial interest in a global security that is exchangeable under the circumstances described in the preceding sentence will be exchangeable for securities in definitive certificated form registered in the names that the depository directs. It is expected that these directions will be based upon directions received by the depository from its participants with respect to ownership of beneficial interests in the global securities.

Euroclear and Clearstream

If so provided in the applicable prospectus supplement, you may hold interests in a global security through Clearstream Banking S.A., which we refer to as “Clearstream,” or Euroclear Bank S.A./N.V., as operator of the Euroclear System, which we refer to as “Euroclear,” either directly if you are a participant in Clearstream or Euroclear or indirectly through organizations which are participants in Clearstream or Euroclear. Clearstream and Euroclear will hold interests on behalf of their respective participants through customers’ securities accounts in the names of Clearstream and Euroclear, respectively, on the books of their respective U.S. depositories, which in turn will hold such interests in customers’ securities accounts in such depositories’ names on DTC’s books.

Clearstream and Euroclear are securities clearance systems in Europe. Clearstream and Euroclear hold securities for their respective participating organizations and facilitate the clearance and settlement of securities transactions between those participants through electronic book-entry changes in their accounts, thereby eliminating the need for physical movement of certificates.

Payments, deliveries, transfers, exchanges, notices and other matters relating to beneficial interests in global securities owned through Euroclear or Clearstream must comply with the rules and procedures of those systems. Transactions between participants in Euroclear or Clearstream, on one hand, and other participants in DTC, on the other hand, are also subject to DTC’s rules and procedures.

Investors will be able to make and receive through Euroclear and Clearstream payments, deliveries, transfers and other transactions involving any beneficial interests in global securities held through those systems only on days when those systems are open for business. Those systems may not be open for business on days when banks, brokers and other institutions are open for business in the United States.

Cross-market transfers between participants in DTC, on the one hand, and participants in Euroclear or Clearstream, on the other hand, will be effected through DTC in accordance with the DTC’s rules on behalf of Euroclear or Clearstream, as the case may be, by their respective U.S. depositories; however, such cross-market transactions will require delivery of instructions to Euroclear or Clearstream, as the case may be, by the counterparty in such system in accordance with the rules and procedures and within the established deadlines (European time) of such system. Euroclear or Clearstream, as the case may be, will, if the transaction meets its settlement requirements, deliver instructions to its U.S. depository to take action to effect final settlement on its behalf by delivering or receiving interests in the global securities through DTC, and making or receiving payment in accordance with normal procedures for same-day fund settlement. Participants in Euroclear or Clearstream may not deliver instructions directly to their respective U.S. depositories.

Due to time zone differences, the securities accounts of a participant in Euroclear or Clearstream purchasing an interest in a global security from a direct participant in DTC will be credited, and any such crediting will be reported to the relevant participant in Euroclear or Clearstream, during the securities settlement processing day (which must be a business day for Euroclear or Clearstream) immediately following the settlement date of DTC. Cash received in Euroclear or Clearstream as a result of sales of interests in a global security by or through a participant in Euroclear or Clearstream to a direct participant in DTC will be received with value on the settlement date of DTC but will be available in the relevant Euroclear or Clearstream cash account only as of the business day for Euroclear or Clearstream following DTC’s settlement date.

Other

The information in this section of this prospectus concerning DTC, Clearstream, Euroclear and their respective book-entry systems has been obtained from sources that we believe to be reliable, but we do not

take responsibility for this information. This information has been provided solely as a matter of convenience. The rules and procedures of DTC, Clearstream and Euroclear are solely within the control of those organizations and could change at any time. Neither we nor the trustee nor any agent of ours or of the trustee has any control over those entities and none of us takes any responsibility for their activities. You are urged to contact DTC, Clearstream and Euroclear or their respective participants directly to discuss those matters. In addition, although we expect that DTC, Clearstream and Euroclear will perform the foregoing procedures, none of them is under any obligation to perform or continue to perform such procedures and such procedures may be discontinued at any time. Neither we nor any agent of ours will have any responsibility for the performance or nonperformance by DTC, Clearstream and Euroclear or their respective participants of these or any other rules or procedures governing their respective operations.

PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods or through underwriters or dealers, through agents and/or directly to one or more purchasers. The securities may be distributed from time to time in one or more transactions:

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

Each time that we sell securities covered by this prospectus, we will provide a prospectus supplement or supplements that will describe the method of distribution and set forth the terms and conditions of the offering of such securities, including the offering price of the securities and the proceeds to us, if applicable.

Offers to purchase the securities being offered by this prospectus may be solicited directly. Agents may also be designated to solicit offers to purchase the securities from time to time. Any agent involved in the offer or sale of our securities will be identified in a prospectus supplement.

If a dealer is utilized in the sale of the securities being offered by this prospectus, the securities will be sold to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale.

If an underwriter is utilized in the sale of the securities being offered by this prospectus, an underwriting agreement will be executed with the underwriter at the time of sale and the name of any underwriter will be provided in the prospectus supplement that the underwriter will use to make resales of the securities to the public. In connection with the sale of the securities, we or the purchasers of securities for whom the underwriter may act as agent, may compensate the underwriter in the form of underwriting discounts or commissions. The underwriter may sell the securities to or through dealers, and those dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters and/or commissions from the purchasers for which they may act as agent. Unless otherwise indicated in a prospectus supplement, an agent will be acting on a best efforts basis and a dealer will purchase securities as a principal, and may then resell the securities at varying prices to be determined by the dealer.

Any compensation paid to underwriters, dealers or agents in connection with the offering of the securities, and any discounts, concessions or commissions allowed by underwriters to participating dealers will be provided in the applicable prospectus supplement. Underwriters, dealers and agents participating in the distribution of the securities may be deemed to be underwriters within the meaning of the Securities Act of 1933, as amended, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions. We may enter into agreements to indemnify underwriters, dealers and agents against civil liabilities, including liabilities under the Securities Act, or to contribute to payments they may be required to make in respect thereof and to reimburse those persons for certain expenses.

Any common stock will be listed on The Nasdaq Global Select Market, but any other securities may or may not be listed on a national securities exchange. To facilitate the offering of securities, certain persons participating in the offering may engage in transactions that stabilize, maintain or otherwise affect the price of the securities. This may include over-allotments or short sales of the securities, which involve the sale by persons participating in the offering of more securities than were sold to them. In these circumstances, these persons would cover such over-allotments or short positions by making purchases in the open market or by exercising their over-allotment option, if any. In addition, these persons may stabilize or maintain the price of the securities by bidding for or purchasing securities in the open market or by imposing penalty bids, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if securities sold by them are repurchased in connection with stabilization transactions. The effect of these transactions may be to stabilize or maintain the market price of the securities at a level above that which might otherwise prevail in the open market. These transactions may be discontinued 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.

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

The 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.

LEGAL MATTERS

Latham & Watkins LLP will pass upon certain legal matters relating to the issuance and sale of the securities offered hereby on behalf of Praxis Precision Medicines, Inc. Additional legal matters may be passed upon for us or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The consolidated financial statements of Praxis Precision Medicines, Inc. appearing in Praxis Precision Medicines, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2021, and the effectiveness of Praxis Precision Medicine, Inc.'s internal control over financial reporting as of December 31, 2021, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their reports thereon included therein, and incorporated herein by reference. Such financial statements are, and audited financial statements to be included in subsequently filed documents will be, incorporated herein in reliance upon the reports of Ernst & Young LLP pertaining to such financial statements and the effectiveness of our internal control over financial reporting as of the respective dates (to the extent covered by consents filed with the Securities and Exchange Commission) given on the authority of such firm as experts in accounting and auditing.

PROSPECTUS SUPPLEMENT

**Up to \$95,573,843.36****Common Stock**

We have entered into an Open Market Sale AgreementSM, or the sales agreement, with Jefferies LLC, or Jefferies, relating to shares of our common stock, par value \$0.0001 per share, offered by this prospectus. In accordance with the terms of the sales agreement, under this prospectus supplement, we may offer and sell shares of our common stock having an aggregate offering price of up to \$95,573,843.36 from time to time through Jefferies, acting as our agent, or the ATM Program. As of the date of this prospectus supplement, we have sold \$29,426,156.64 of \$125,000,000 under the ATM Program. We are registering the offer and sale of the remaining \$95,573,843.36 that has not been sold under the ATM Program.

Our common stock is listed on The Nasdaq Global Select Market under the symbol "PRAX". On February 3, 2023, the closing price of our common stock, as reported on The Nasdaq Global Select Market, was \$4.64 per share.

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

Jefferies will be entitled to compensation at a commission rate of 3.0% of the gross sales price of common stock sold under the sales agreement. See "Plan of Distribution" beginning on page [S-12](#) for additional information regarding the compensation to be paid to Jefferies. In connection with the sale of the common stock on our behalf, Jefferies will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of Jefferies will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to Jefferies with respect to certain liabilities, including liabilities under the Securities Act and the Securities Exchange Act of 1934, as amended, or the Exchange Act.

Investing in our common stock involves a high degree of risk. You should review carefully the risks and uncertainties referenced under the heading "Risk Factors" on page [S-5](#) of this prospectus and in the documents that are incorporated by reference into this prospectus.

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

Jefferies

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We are responsible for the information contained and incorporated by reference in this prospectus supplement, the accompanying base prospectus and in any related free writing prospectus we prepare or authorize. We have not authorized anyone to give you any other information, and we take no responsibility for any other information that others may give you. If you are in a jurisdiction where offers to sell, or solicitations of offers to purchase, the securities offered by this documentation are unlawful, or if you are a person to whom it is unlawful to direct these types of activities, then the offer presented in this document does not extend to you. The information contained in this document speaks only as of the date of this document, unless the information specifically indicates that another date applies. Our business, financial condition, results of operations and prospects may have changed since those dates.

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement is part of a registration statement that we have filed with the Securities and Exchange Commission, or SEC, utilizing a “shelf” registration process, and relates to the offering of our common stock.

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

You should rely only on the information contained or incorporated by reference in this prospectus, the accompanying base prospectus and any free writing prospectus we may authorize for use in connection with this offering. We have not, and Jefferies has not, authorized anyone to provide you with different information. We and Jefferies take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may provide.

The information contained in this prospectus, the accompanying base prospectus, the documents incorporated by reference herein or therein and any free writing prospectus we may authorize for use in connection with this offering, is accurate only as of their respective dates, regardless of the time of delivery of any such document or the time of any sale of our common stock. Our business, financial condition, results of operations and prospects may have changed since those dates. It is important for you to read and consider all information contained in this prospectus supplement, the accompanying base prospectus, the documents incorporated by reference herein and therein and any free writing prospectus that we have authorized for use in connection with this offering, in making your investment decision. You should read this prospectus and the accompanying base prospectus, as well as the documents incorporated by reference herein and therein, the additional information described under the section titled “Where You Can Find More Information” and “Incorporation of Certain Documents by Reference” in this prospectus supplement, and any free writing prospectus that we have authorized for use in connection with this offering, before investing in our common stock.

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 in this prospectus supplement were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

This prospectus supplement and the documents incorporated by reference herein also contain estimates, projections and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. 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 reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data 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.

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

As used in this prospectus, unless the context otherwise requires, references to the “Company,” “Praxis,” “we,” “us” and “our” refer to Praxis Precision Medicines, Inc. and its consolidated subsidiaries.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information and does not contain all of the information that you should consider in making your investment decision. Before investing in our common stock, you should carefully read this entire prospectus, the accompanying base prospectus and any free writing prospectus that we have authorized for use in connection with this offering carefully, including the information in our filings with the U.S. Securities and Exchange Commission, or the SEC, incorporated by reference in this prospectus supplement.

Our Company

We are a clinical-stage biopharmaceutical company translating insights from genetic epilepsies into the development of therapies for central nervous system, or CNS, disorders characterized by neuronal excitation-inhibition imbalance. Normal brain function requires a delicate balance of excitation and inhibition in neuronal circuits, which, when dysregulated, can lead to abnormal function and both rare and more prevalent neurological disorders. We are applying genetic insights to the discovery and development of therapies for neurological disorders through two proprietary platforms, using our understanding of shared biological targets and circuits in the brain. Each platform currently has multiple programs, with significant potential for additional program and indication expansion:

- **Cerebrum**[™], our small molecule platform, utilizes deep understanding of neuronal excitability and neuronal networks and applies a series of computational and experimental tools to develop orally available precision therapies
- **Solidus**[™], our antisense oligonucleotide, or ASO, platform, is an efficient, targeted precision medicine discovery and development engine anchored on a proprietary, computational methodology

Our platforms utilize a deliberate, pragmatic and patient-guided approach, leveraging a suite of translational tools, including novel transgenic and predictive translational animal models and electrophysiology markers, to enable an efficient path to proof-of-concept in patients. Through this approach, we have established a diversified, multimodal CNS portfolio with four clinical-stage product candidates across movement disorders and epilepsy.

Corporate Information

We were incorporated under the laws of the State of Delaware on September 22, 2015. Our principal executive office is located at 99 High Street, 30th Floor, Boston, MA 02110, and our telephone number is (617) 300-8460. Our website address is www.praxismedicines.com. We do not incorporate the information on or accessible through our website into this prospectus supplement, and you should not consider any information on, or that can be accessed through, our website as part of this prospectus supplement.

THE OFFERING

Common stock offered by us:	Shares of our common stock having an aggregate offering price of up to \$95,573,843.36.
Common stock to be outstanding immediately after this offering	Up to 69,980,264 shares of our common stock, assuming sales of 20,597,811 shares of our common stock in this offering at a public offering price of \$4.64 per share, which was the last reported sale price per share of our common stock on The Nasdaq Global Select Market on February 3, 2023. The actual number of shares of our common stock issued will vary depending on the sales price under this offering.
Plan of Distribution:	“At the market offering” that may be made from time to time on The Nasdaq Global Select Market or other existing trading market for our common stock through Jefferies, as sales agent. See “Plan of Distribution” on page S-12 of this prospectus.
Use of Proceeds:	Our management will retain broad discretion regarding the allocation and use of the net proceeds. We currently intend to use the net proceeds from this offering, together with our existing cash, cash equivalents and marketable securities, to fund research and clinical development of current or additional product candidates, including commercial readiness activities, and the remainder for working capital and other general corporate purposes. See “Use of Proceeds” on page S-9 of this prospectus.
Risk Factors:	Investing in our common stock involves significant risks. See “Risk Factors” on page S-5 of this prospectus and under similar headings in the documents incorporated by reference into this prospectus for a discussion of the factors you should carefully consider before deciding to invest in our common stock.
The Nasdaq Global Select Market symbol:	“PRAX”

The number of shares of common stock to be outstanding after this offering is based on 49,382,453 shares of common stock outstanding as of December 31, 2022 and excludes:

- 8,838,028 shares of our common stock issuable upon the exercise of stock options outstanding as of December 31, 2022 under our 2017 Stock Incentive Plan and 2020 Stock Option and Incentive Plan, at a weighted average exercise price of \$13.93 per share;
- 1,650,955 shares of our common stock reserved for future issuance under our 2020 Stock Option and Incentive Plan as of December 31, 2022;
- 839,922 shares of our common stock reserved for future issuance under the 2020 Employee Stock Purchase Plan as of December 31, 2022; and
- 743,950 shares of our common stock reserved for future vesting of restricted stock units as of December 31, 2022.

Unless otherwise indicated, all information in this prospectus supplement assumes no exercise of outstanding stock options or vesting of restricted stock units described above.

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before making an investment decision, you should carefully consider the risks described below and in our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q or Current Reports on Form 8-K, as well as any amendments thereto reflected in subsequent filings with the SEC, each of which are incorporated by reference in this prospectus supplement, and all of the other information in this prospectus supplement, including our financial statements and related notes incorporated by reference herein. If any of these risks is realized, our business, financial condition, results of operations and prospects could be materially and adversely affected. In that event, the trading price of our common stock could decline and you could lose part or all of your investment. Additional risks and uncertainties that are not yet identified or that we currently believe to be immaterial may also materially harm our business, financial condition, results of operations and prospects and could result in a complete loss of your investment.

Risks Related To This Offering

We have broad discretion in the use of the net proceeds from this offering and may invest or spend the proceeds in ways with which you do not agree and in ways that may not yield a return on your investment.

Our management will have broad discretion in the application of the net proceeds from this offering, including for any of the purposes described in the section titled "Use of Proceeds," and you will be relying on the judgment of our management regarding such application. You will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used effectively. Our management might not apply the net proceeds in ways that ultimately increase the value of your investment. If we do not invest or apply the net proceeds from this offering in ways that enhance stockholder value, we may fail to achieve expected results, which could cause our stock price to decline. Pending their use, we may invest the net proceeds in a variety of capital preservation instruments, including short-term, investment-grade, interest-bearing instruments and U.S. government securities. These investments may not yield a favorable return to our stockholders.

If you purchase our common stock in this offering, you will incur immediate and substantial dilution in the net tangible book value of your shares.

The offering price per share in this offering may exceed the net tangible book value per share of our common stock outstanding at the time of sale. Assuming that an aggregate of 20,597,811 shares of our common stock are sold at an assumed offering price of \$4.64 per share, the last reported sale price of our common stock on The Nasdaq Global Select Market on February 3, 2023, for aggregate gross proceeds of \$95.6 million, after deducting commissions and estimated offering expenses payable by us, investors in this offering would experience immediate dilution of \$2.23 per share, representing the difference between our as adjusted net tangible book value per share as of December 31, 2022 of \$2.41, after giving effect to this offering, and the assumed offering price.

This dilution is due to the substantially lower price paid by some of our investors who purchased shares prior to this offering as compared to the price offered to the public in this offering and the exercise of stock options granted to our employees, directors and consultants. In addition, we have a significant number of stock options and restricted stock units outstanding. The exercise of any of the outstanding options or the vesting of the restricted stock units would result in further dilution. As a result of the dilution to investors purchasing shares in this offering, investors may receive significantly less than the purchase price paid in this offering, if anything, in the event of our liquidation. Further, because we expect we will need to raise additional capital to fund our future activities, we may in the future sell substantial amounts of common stock or securities convertible into or exchangeable for common stock.

Future issuances of common stock or common stock-related securities, together with the exercise of outstanding stock options, if any, may result in further dilution. For a further description of the dilution that you will experience immediately after this offering, see the section titled "Dilution."

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

Additional capital will be needed in the future to continue our planned operations. To the extent we issue additional equity securities to raise capital or pursuant to our equity incentive plans or other contractual

obligations, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell or issue common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

In addition, sales of a substantial number of shares of our outstanding common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. Persons who were our stockholders prior to our initial public offering continue to hold a substantial number of shares of our common stock that many of them are now able to sell in the public market. Significant portions of these shares are held by a relatively small number of stockholders. Sales by our stockholders of a substantial number of shares, or the expectation that such sales may occur, could significantly reduce the market price of our common stock.

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

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

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

Investors who purchase shares in this offering at different times will likely pay different prices, and so may experience different outcomes in their investment results. We will have discretion, subject to market demand, to vary the timing, prices, and numbers of shares sold, and there is no minimum or maximum sales price. Investors may experience a decline in the value of their shares as a result of share sales made at prices lower than the prices they paid.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying base prospectus, the documents that we incorporate by reference herein or therein, and any related free writing prospectus contain 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, or the Exchange Act. Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. These statements are often, but are not always, made through the use of words or phrases such as “may,” “will,” “could,” “should,” “expects,” “intends,” “plans,” “anticipates,” “believes,” “estimates,” “predicts,” “projects,” “potential,” “continue,” and similar expressions, or the negative of these terms, or similar expressions. Accordingly, these statements involve estimates, assumptions, risks and uncertainties which could cause actual results to differ materially from those expressed in them. Any forward-looking statements are qualified in their entirety by reference to the factors discussed throughout this prospectus supplement, the accompanying base prospectus and the documents incorporated by reference herein and therein, and in particular those factors referenced in the section “Risk Factors” in this prospectus supplement.

This prospectus supplement, the accompanying base prospectus and the documents incorporated by reference herein and therein contain forward-looking statements that are based on our management’s belief and assumptions and on information available to our management as of their respective dates. These statements relate to future events or our future financial performance, and 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 these forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

- the success, cost and timing of our product candidate development activities and clinical trials;
- our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidates;
- the ability to license additional intellectual property relating to our product candidates from third parties and to comply with our existing license agreements and collaboration agreements;
- the ability and willingness of our third-party research institution collaborators to continue research and development activities relating to our product candidates;
- our ability to commercialize our product candidates, if approved, in light of the intellectual property rights of others;
- our ability to obtain funding for our operations, including funding necessary to complete further development and, if approved, commercialization of our product candidates;
- the commercialization of our product candidates, if approved;
- our plans to research, develop and, if approved, commercialize our product candidates;
- future agreements with third parties in connection with the commercialization of our product candidates, if approved, and any other approved product;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- the rate and degree of market acceptance of our product candidates, if approved;
- the pricing and reimbursement of our product candidates, if approved;
- regulatory developments in the United States and foreign countries;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- the success of competing therapies that are or may become available;
- our ability to attract and retain key scientific or management personnel;
- the accuracy of our estimates regarding expenses, future revenue, capital requirements and needs for additional financing; and
- our intended use of proceeds for this offering.

These forward-looking statements are neither promises nor guarantees of future performance due to a variety of risks and uncertainties, many of which are beyond our control, which could cause actual results to differ materially from those indicated by these forward-looking statements, including, without limitation 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 period ended December 31, 2021 and our most recent Quarterly Reports on Form 10-Q for the quarters ended March 31, 2022, June 30, 2022 and September 30, 2022, and our Current Reports on Form 8-K, and the section in this prospectus supplement entitled “Risk Factors.”

The forward-looking statements in this prospectus supplement, the accompanying base prospectus and the documents incorporated by reference herein and therein represent our views as of their respective dates. 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 assume no obligation to update or revise any forward-looking statements 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 dates on which they were made.

This prospectus supplement, the accompanying base prospectus and the documents incorporated by reference herein and therein also contain estimates, projections and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. 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 reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data 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.

USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate gross sales proceeds of up to \$95.6 million from time to time. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. There can be no assurance that we will sell any shares under or fully utilize our sales agreement with Jefferies as a source of financing.

We currently intend to use the net proceeds from this offering, together with our existing cash, cash equivalents and marketable securities, to fund research and clinical development of current or additional product candidates, including commercial readiness activities, and the remainder for working capital and other general corporate purposes. The expected use of the net proceeds from this offering, if any, 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 will depend on numerous factors, including the factors described under "Risk Factors" in this prospectus supplement, the accompanying base prospectus and in the documents incorporated by reference herein and therein, as well as the amount of cash used in our operations. We may find it necessary or advisable to use the net proceeds for other purposes, and we will have broad discretion in the application of the net proceeds. Pending the uses described above, we may invest the net proceeds in a variety of capital preservation instruments, including short-term, investment-grade, interest-bearing instruments and U.S. government securities.

DIVIDEND POLICY

We have never declared or paid cash dividends on our capital stock. We intend to retain all available funds and any future earnings to fund the growth and development of our business. We do not intend to pay cash dividends to our stockholders in the foreseeable future. In addition, any future financing instruments could preclude us from paying dividends. Any future determination to pay dividends will be made at the discretion of our board of directors subject to applicable laws, and will depend upon, among other factors, our results of operations, financial condition, contractual restrictions and capital requirements. Investors should not purchase our common stock with the expectation of receiving cash dividends.

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 in this offering and the as adjusted net tangible book value per share of our common stock immediately after this offering. Our net tangible book value as of December 31, 2022 was approximately \$76.1 million, or approximately \$1.54 per share of common stock. Net tangible book value per share represents the amount of total tangible assets (total assets less intangible assets) less total liabilities, divided by the number of shares of our common stock outstanding as of December 31, 2022.

Dilution in net tangible book value per share to new investors participating in this offering represents the difference between the amount per share paid by purchasers in this offering and the as adjusted net tangible book value per share of our common stock immediately after giving effect to this offering. After giving effect to the assumed sale of 20,597,811 shares of our common stock in the aggregate amount of approximately \$95.6 million at an assumed offering price of \$4.64 per share, the last reported sale price of our common stock on February 3, 2023, and after deducting commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of December 31, 2022 would have been approximately \$168.6 million, or approximately \$2.41 per share of common stock. This represents an immediate increase in net tangible book value of \$0.87 per share of common stock to our existing stockholders and immediate dilution in net tangible book value of \$2.23 per share of common stock to investors participating in this offering at the assumed offering price.

Dilution per share to new investors is determined by subtracting as adjusted net tangible book value per share after this offering from the assumed public offering price per share paid by new investors. The following table illustrates this per share dilution:

Assumed public offering price per share	\$ 4.64
Historical net tangible book value per share as of December 31, 2022	\$ 1.54
Increase in net tangible book value per share attributable to new investors participating in this offering	<u>\$ 0.87</u>
As adjusted net tangible book value per share as of December 31, 2022 after this offering	\$ 2.41
Dilution per share to new investors participating in this offering	\$ 2.23

The information above and in the foregoing table is based upon 49,382,453 shares of our common stock outstanding as of December 31, 2022. The information above and in the foregoing table excludes:

- 8,838,028 shares of our common stock issuable upon the exercise of stock options outstanding as of December 31, 2022 under our 2017 Stock Incentive Plan and 2020 Stock Option and Incentive Plan, at a weighted average exercise price of \$13.93 per share;
- 1,650,955 shares of our common stock reserved for future issuance under our 2020 Stock Option and Incentive Plan as of December 31, 2022;
- 839,922 shares of our common stock reserved for future issuance under the 2020 Employee Stock Purchase Plan as of December 31, 2022; and
- 743,950 shares of our common stock reserved for future vesting of restricted stock units as of December 31, 2022.

In addition, we may choose to raise additional capital in the future through the sale of equity or convertible debt securities 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 any of our outstanding options are exercised, any of our restricted stock units vest, new options or restricted stock units are issued under our equity incentive plans or we issue additional shares of common stock or other equity or convertible debt securities in the future, there will be further dilution to investors participating in this offering.

PLAN OF DISTRIBUTION

We have entered into a sales agreement with Jefferies, under which we may offer and sell up to \$125,000,000 of shares of our common stock from time to time through Jefferies acting as agent, or the ATM Program. As of the date of this prospectus supplement, we have sold \$29,426,156.64 under the ATM Program. We are registering the offer and sale of the remaining \$95,573,843.36 that has not been sold under the ATM Program. Sales of shares of our common stock, if any, under this prospectus supplement and the accompanying base prospectus will be made by any method that is deemed to be an "at the market offering" as defined in Rule 415(a)(4) under the Securities Act.

Each time we wish to issue and sell shares of our common stock under the sales agreement, we will notify Jefferies of the number of shares to be sold, the dates on which such sales are anticipated to be made, any limitation on the number of shares to be sold in any one day and any minimum price below which sales may not be made. Once we have so instructed Jefferies, unless Jefferies declines to accept the terms of such notice, Jefferies has agreed to use its commercially reasonable efforts consistent with its normal trading and sales practices to sell such shares up to the amount specified on such terms. The obligations of Jefferies under the sales agreement to sell the shares of our common stock are subject to a number of conditions that we must meet.

The settlement of sales of shares between us and Jefferies is generally anticipated to occur on the second trading day following the date on which the sale was made. Sales of our common stock as contemplated in this prospectus supplement will be settled through the facilities of The Depository Trust Company or by such other means as we and Jefferies may agree upon. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

We will pay Jefferies a commission equal to 3.0% of the aggregate gross proceeds we receive from each sale of shares of our common stock. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. We have agreed to reimburse Jefferies for the fees and disbursements of its counsel, payable upon execution of the sales agreement, in an amount not to exceed \$75,000, in addition to certain ongoing disbursements of its legal counsel. We estimate that the total expenses for the offering, excluding any commissions or expense reimbursement payable to Jefferies under the terms of the sales agreement, will be approximately \$0.4 million. The remaining proceeds, after deducting any other transaction fees, will equal our net proceeds from the sale of shares of our common stock in this offering.

Jefferies will provide written confirmation to us before the open on The Nasdaq Global Select Market on the day following each day on which shares of our common stock are sold under the sales agreement. Each confirmation will include the number of shares sold on that day, the aggregate gross proceeds of such sales and the proceeds to us.

In connection with the sale of shares of our common stock on our behalf, Jefferies may be deemed to be an "underwriter" within the meaning of the Securities Act, and the compensation of Jefferies will be deemed to be underwriting commissions or discounts. We have agreed to indemnify Jefferies against certain liabilities, including civil liabilities under the Securities Act. We have also agreed to contribute to payments Jefferies may be required to make in respect of such liabilities.

The offering of shares of our common stock pursuant to the sales agreement will terminate upon the earlier of (i) the sale of all shares of our common stock subject to the sales agreement and (ii) the termination of the sales agreement as permitted therein. We and Jefferies may terminate the sales agreement at any time upon ten days' prior notice.

This summary of the material provisions of the sales agreement does not purport to be a complete statement of its terms and conditions. A copy of the sales agreement is filed as an exhibit to the registration statement of which this prospectus supplement forms a part.

Jefferies and its affiliates may in the future provide various investment banking, commercial banking, financial advisory and other financial services for us and our affiliates, for which services they may in the

future receive customary fees. In the course of its business, Jefferies may actively trade our securities for its own account or for the accounts of customers, and, accordingly, Jefferies may at any time hold long or short positions in such securities.

The prospectus supplement and the accompanying base prospectus in electronic format may be made available on a website maintained by Jefferies, and Jefferies may distribute this prospectus supplement and the accompanying base prospectus electronically.

LEGAL MATTERS

Latham & Watkins LLP will pass upon certain legal matters relating to the issuance and sale of the securities offered hereby on behalf of Praxis Precision Medicines, Inc. Certain legal matters will be passed upon for Jefferies LLC by Mintz, Levin, Cohn, Ferris, Glovsky & Popeo, P.C.

EXPERTS

The consolidated financial statements of Praxis Precision Medicines, Inc. appearing in Praxis Precision Medicines, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2021, and the effectiveness of Praxis Precision Medicine, Inc.'s internal control over financial reporting as of December 31, 2021, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their reports thereon included therein, and incorporated herein by reference. Such financial statements are, and audited financial statements to be included in subsequently filed documents will be, incorporated herein in reliance upon the reports of Ernst & Young LLP pertaining to such financial statements and the effectiveness of our internal control over financial reporting as of the respective dates (to the extent covered by consents filed with the Securities and Exchange Commission) given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus supplement is part of a registration statement on Form S-3 that we have filed with the SEC. This prospectus supplement, filed as part of the registration statement, does not contain all the information set forth in the registration statement and its exhibits and schedules, portions of which have been omitted as permitted by the rules and regulations of the SEC. For further information about us, we refer you to the registration statement and to its exhibits and schedules. Certain information in the registration statement has been omitted from this prospectus supplement in accordance with the rules of the SEC.

We are subject to the reporting and information requirements of the Exchange Act and, in accordance therewith, file annual, quarterly and special reports, proxy statements and other information with the SEC. These documents also may be accessed through the SEC's electronic data gathering, analysis and retrieval system, or EDGAR, via electronic means, including the SEC's home page on the Internet (www.sec.gov). Written requests for such copies should be directed to Praxis Precision Medicines, Inc., 99 High Street, 30th Floor, Boston, Massachusetts 02110, telephone: (617) 300-8460 and our website is located at www.praxismedicines.com. Information contained on our website is not incorporated by reference into this prospectus supplement and, therefore, is not part of this prospectus supplement.

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" in the accompanying base prospectus. 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 shareholder upon request and without charge.

INCORPORATION BY REFERENCE

The SEC allows us to incorporate by reference the information and reports we file with it, which means that we can disclose important information to you by referring you to these documents. The information incorporated by reference is an important part of this prospectus, and information that we file later with the SEC will automatically update and supersede the information already incorporated by reference. We are incorporating by reference the documents listed below, which we have already filed with the SEC (SEC File No. 001-39620), 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 this prospectus, 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 year ended December 31, 2021, filed with the SEC on February 28, 2022;](#)
- [our Definitive Proxy Statement filed with the SEC on April 14, 2022, to the extent information therein is filed and not furnished;](#)
- Quarterly Reports on Form 10-Q for the quarters ended March 31, 2022, June 30, 2022 and September 30, 2022, filed with the SEC on [May 9, 2022](#), [August 8, 2022](#) and [November 9, 2022](#), respectively;
- Current Reports on Form 8-K and Amended Current Reports on Form 8-K/A filed with the SEC on [January 7, 2022](#), [January 10, 2022](#) (Item 8.01 only), [April 29, 2022](#), [May 9, 2022](#) (Item 8.01 only), [May 23, 2022](#), [June 1, 2022](#), [June 6, 2022](#), [July 11, 2022](#), [July 26, 2022](#), [August 8, 2022](#) (Item 8.01 only), [August 12, 2022](#), [September 7, 2022](#) and [November 28, 2022](#) (Item 8.01 only);
- [the description of our common stock contained in our Registration Statement on Form 8-A filed with the SEC on October 14, 2020, including any amendments or reports filed for the purposes of updating this description.](#)

Upon request, we will provide, without charge, to each person, including any beneficial owner, to whom a copy of this prospectus supplement is delivered, a copy of the documents incorporated by reference into this prospectus supplement but not delivered with the prospectus supplement. You may request a copy of these filings, and any exhibits we have specifically incorporated by reference as an exhibit in this prospectus, at no cost by writing or telephoning us at the following address: Praxis Precision Medicines, Inc., 99 High Street, 30th Floor, Boston, Massachusetts 02110, telephone: (617) 300-8460.

You may also access these documents, free of charge on the SEC's website at www.sec.gov or on our website at www.praxismedicines.com. Information contained on our website is not incorporated by reference into this prospectus supplement, and you should not consider any information on, or that can be accessed from, our website as part of this prospectus supplement.

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 supplement or the registration statement of which this prospectus supplement is a part.

This prospectus supplement 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 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 supplement 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.

Any statement contained in a document that is incorporated by reference will be modified or superseded for all purposes to the extent that a statement contained in this prospectus supplement, or in any other document that is subsequently filed with the SEC and incorporated by reference into this prospectus supplement, modifies or is contrary to that previous statement. Any statement so modified or superseded will not be deemed

a part of this prospectus supplement, except as so modified or superseded. Since information that we later file with the SEC will update and supersede previously incorporated information, you should look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus supplement or in any documents previously incorporated by reference have been modified or superseded.



Up to \$95,573,843.36

Common Stock

PROSPECTUS SUPPLEMENT

Jefferies

February 7, 2023

PART II
INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. *Other Expenses of Issuance and Distribution*

The following is an estimate of the expenses (all of which are to be paid by the registrant) that we may incur in connection with the securities being registered hereby.

SEC registration fee	\$ 33,060
FINRA filing fee	\$225,500
Printing expenses	\$ (1)
Legal fees and expenses	\$ (1)
Accounting fees and expenses	\$ (1)
Blue Sky, qualification fees and expenses	\$ (1)
Transfer agent fees and expenses	\$ (1)
Trustee fees and expenses	\$ (1)
Warrant agent fees and expenses	\$ (1)
Miscellaneous	\$ (1)
Total	\$ (1)

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- (1) These fees are calculated based on the securities offered and the number of issuances and accordingly cannot be estimated at this time.

Item 15. *Indemnification of Directors and Officers*

Subsection (a) of Section 145 of the General Corporation Law of the State of Delaware, or the DGCL, empowers a corporation to indemnify any person who was or is a party or who is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of the corporation) by reason of the fact that the person is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by the person in connection with such action, suit or proceeding if the person acted in good faith and in a manner the person reasonably believed to be in or not opposed to the best interests of the corporation, and, with respect to any criminal action or proceeding, had no reasonable cause to believe the person's conduct was unlawful.

Subsection (b) of Section 145 empowers a corporation to indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the corporation to procure a judgment in its favor by reason of the fact that the person acted in any of the capacities set forth above, against expenses (including attorneys' fees) actually and reasonably incurred by the person in connection with the defense or settlement of such action or suit if the person acted in good faith and in a manner the person reasonably believed to be in or not opposed to the best interests of the corporation, except that no indemnification shall be made in respect of any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or the court in which such action or suit was brought shall determine upon application that, despite the adjudication of liability but in view of all the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which the Court of Chancery or such other court shall deem proper.

Section 145 further provides that to the extent a director or officer of a corporation has been successful on the merits or otherwise in the defense of any action, suit or proceeding referred to in subsections (a) and (b) of Section 145, or in defense of any claim, issue or matter therein, such person shall be indemnified against expenses (including attorneys' fees) actually and reasonably incurred by such person in connection therewith; that indemnification provided for by Section 145 shall not be deemed exclusive of any other rights

to which the indemnified party may be entitled; and the indemnification provided for by Section 145 shall, unless otherwise provided when authorized or ratified, continue as to a person who has ceased to be a director, officer, employee or agent and shall inure to the benefit of such person's heirs, executors and administrators. Section 145 also empowers the corporation to purchase and maintain insurance on behalf of any person who is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise against any liability asserted against such person and incurred by such person in any such capacity, or arising out of his status as such, whether or not the corporation would have the power to indemnify such person against such liabilities under Section 145.

Section 102(b)(7) of the DGCL provides that a corporation's certificate of incorporation may contain a provision eliminating or limiting the personal liability of a director to the corporation or its stockholders for monetary damages for breach of fiduciary duty as a director, provided that such provision shall not eliminate or limit the liability of a director (i) for any breach of the director's duty of loyalty to the corporation or its stockholders, (ii) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (iii) under Section 174 of the DGCL, or (iv) for any transaction from which the director derived an improper personal benefit.

Any underwriting agreement or distribution agreement that the registrant enters into with any underwriters or agents involved in the offering or sale of any securities registered hereby may require such underwriters or dealers to indemnify the registrant, some or all of its directors and officers and its controlling persons, if any, for specified liabilities, which may include liabilities under the Securities Act of 1933, as amended, or the Securities Act.

We have adopted provisions in our fourth certificate of incorporation and amended and restated by-laws that limit or eliminate the personal liability of our directors to the fullest extent permitted by the DGCL, as it now exists or may in the future be amended. Consequently, a director will not be personally liable to us or our stockholders for monetary damages or breach of fiduciary duty as a director, except for liability for:

- any breach of the director's duty of loyalty to us or our stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- any unlawful payments related to dividends or unlawful stock purchases, redemptions or other distributions; or
- any transaction from which the director derived an improper personal benefit.

These limitations of liability do not alter director liability under the federal securities laws and do not affect the availability of equitable remedies such as an injunction or rescission.

In addition, the by-laws provide that:

- we will indemnify our directors, officers and, in the discretion of our board of directors, certain employees to the fullest extent permitted by the DGCL, as it now exists or may in the future be amended; and
- we will advance reasonable expenses, including attorneys' fees, to our directors and, in the discretion of our board of directors, to our officers and certain employees, in connection with legal proceedings relating to their service for or on behalf of us, subject to limited exceptions.

We have entered into indemnification agreements with each of our directors and our executive officers. These agreements provide that we will indemnify each of our directors, our executive officers and, at times, their affiliates to the fullest extent permitted by Delaware law. We will advance expenses, including attorneys' fees (but excluding judgments, fines and settlement amounts), to each indemnified director, executive officer or affiliate in connection with any proceeding in which indemnification is available and we will indemnify our directors and officers for any action or proceeding arising out of that person's services as a director or officer brought on behalf of us or in furtherance of our rights. Additionally, certain of our directors or officers may have certain rights to indemnification, advancement of expenses or insurance

provided by their affiliates or other third parties, which indemnification relates to and might apply to the same proceedings arising out of such director's or officer's services as a director referenced herein. Nonetheless, we have agreed in the indemnification agreements that our obligations to those same directors or officers are primary and any obligation of such affiliates or other third parties to advance expenses or to provide indemnification for the expenses or liabilities incurred by those directors are secondary.

We also maintain general liability insurance which covers certain liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers, including liabilities under the Securities Act.

Item 16. Exhibits

Exhibit Number	Description
1.1*	Form of Underwriting Agreement.
1.2***	Open Market Sale Agreement, dated as of November 3, 2021 between Praxis Precision Medicines, Inc. and Jefferies LLC.
3.1	Amended and Restated Certificate of Incorporation of Praxis Precision Medicines, Inc. (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-39620) filed on October 20, 2020).
3.2	Amended and Restated Bylaws of Praxis Precision Medicines, Inc. (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-39620) filed on January 7, 2022).
4.1***	Fourth Amended and Restated Investors' Rights Agreement among Praxis Precision Medicines, Inc. and certain of its stockholders, effective as of July 24, 2020, as amended.
4.2	Specimen Stock Certificate Evidencing the Shares of Common Stock (incorporated by reference to Exhibit 4.1 to the Registrant's Registration Statement on Form S-1/A (File No. 333-249074) filed on October 9, 2020).
4.3*	Form of Specimen Certificate Representing Preferred Stock.
4.4***	Form of Indenture.
4.5*	Form of Note.
4.6*	Form of Warrant.
4.7*	Form of Warrant Agreement.
4.8*	Form of Unit Agreement.
5.1	Opinion of Latham & Watkins LLP.
23.1	Consent of Latham & Watkins LLP (included in Exhibit 5.1).
23.2	Consent of Ernst & Young LLP, independent registered public accounting firm.
25.1**	Statement of Eligibility on Form T-1 under the Trust Indenture Act of 1939, as amended, of Debt Trustee (to be filed prior to any issuance of Debt Securities).
107	Filing Fee Table

* To be filed by amendment or incorporated by reference in connection with the offering of the securities.

** To be filed in accordance with the requirements of Section 305(b)(2) of the Trust Indenture Act of 1939.

*** Previously filed.

Item 17. Undertakings

(a) The undersigned registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by Section 10(a)(3) of the Securities Act;

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement ; and

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, however, that paragraphs (a)(1)(i), (a)(1)(ii), and (a)(1)(iii) above do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the registrant pursuant to section 13 or section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is a part of the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(5) That, for the purpose of determining liability under the Securities Act to any purchaser:

(A) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(B) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by section 10(a) of the Securities Act shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof. *Provided, however,* that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any

statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

(6) That, for the purpose of determining liability of the registrant under the Securities Act to any purchaser in the initial distribution of the securities:

The undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

- (i) Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;
- (ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;
- (iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and
- (iv) Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.

(b) The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act, each filing of the registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

(h) Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

(j) The undersigned registrant hereby undertakes to file an application for the purpose of determining the eligibility of the trustee to act under subsection (a) of Section 310 of the Trust Indenture Act (the "Act") in accordance with the rules and regulations prescribed by the SEC under section 305(b)(2) of the Act.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Post-Effective Amendment No. 1 to the Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Boston, Massachusetts, on the 7th day of February, 2023.

PRAXIS PRECISION MEDICINES, INC.By: /s/ Marcio Souza

Name: Marcio Souza

Title: Chief Executive Officer

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, this registration statement has been signed below by the following persons on behalf of the registrant in the capacities and on the dates indicated.

<u>SIGNATURE</u>	<u>TITLE</u>	<u>DATE</u>
<u>/s/ Marcio Souza</u> Marcio Souza	Chief Executive Officer and Director (Principal Executive Officer)	February 7, 2023
<u>/s/ Timothy Kelly</u> Timothy Kelly	Chief Financial Officer (Principal Financial Officer)	February 7, 2023
<u>*</u> Lauren Mastrocola	Principal Accounting Officer	February 7, 2023
<u>*</u> Dean Mitchell	Chairman of the Board	February 7, 2023
<u>*</u> Jeffrey Chodakewitz, M.D.	Director	February 7, 2023
<u>*</u> Merit Cudkowicz, M.D.	Director	February 7, 2023
<u>/s/ Jill DeSimone</u> Jill DeSimone	Director	February 7, 2023
<u>*</u> Gregory Norden	Director	February 7, 2023
<u>*</u> William Young	Director	February 7, 2023

* By: /s/ Marcio SouzaMarcio Souza
Attorney-in-Fact

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FIRM / AFFILIATE OFFICES

Austin	Milan
Beijing	Munich
Boston	New York
Brussels	Orange County
Century City	Paris
Chicago	Riyadh
Dubai	San Diego
Düsseldorf	San Francisco
Frankfurt	Seoul
Hamburg	Shanghai
Hong Kong	Silicon Valley
Houston	Singapore
London	Tel Aviv
Los Angeles	Tokyo
Madrid	Washington, D.C.

February 7, 2023

Praxis Precision Medicines, Inc.
 99 High Street, 30th Floor
 Boston, MA 02110

Re: Registration Statement on Form S-3

To the addressee set forth above:

We have acted as special counsel to Praxis Precision Medicines, Inc., a Delaware corporation (the “*Company*”), in connection with its filing on the date hereof with the Securities and Exchange Commission (the “*Commission*”) of a Post-Effective Amendment No. 1 to the Registration Statement on Form S-3 (Registration No. 333-260726) (as amended, the “*Registration Statement*”), including a base prospectus (the “*Base Prospectus*”), which provides that it will be supplemented by one or more prospectus supplements (each such prospectus supplement, together with the Base Prospectus, a “*Prospectus*”), under the Securities Act of 1933, as amended (the “*Act*”), relating to the registration for issue and sale by the Company of up to \$300,000,000 aggregate offering amount of (i) shares of the Company’s common stock, \$0.0001 par value per share (“*Common Stock*”), (ii) shares of one or more series of the Company’s preferred stock, \$0.0001 par value per share (“*Preferred Stock*”), (iii) one or more series of the Company’s debt securities (collectively, “*Debt Securities*”) to be issued under an indenture to be entered into between the Company, as issuer, and a trustee (a form of which is included as Exhibit 4.4 to the Registration Statement) and one or more board resolutions, supplements thereto or officer’s certificates thereunder (such indenture, together with the applicable board resolution, supplement or officer’s certificate pertaining to the applicable series of Debt Securities, the “*Applicable Indenture*”), (iv) warrants (“*Warrants*”), and (v) units (“*Units*”). The Common Stock, Preferred Stock, Debt Securities, Warrants, and Units, plus any additional Common Stock, Preferred Stock, Debt Securities, Warrants, and Units that may be registered pursuant to any subsequent registration statement that the Company may hereafter file with the Commission pursuant to Rule 462(b) under the Act in connection with the offering by the Company contemplated by the Registration Statement, are referred to herein collectively as the “*Securities*.”

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We also have acted as special counsel to the Company in connection with the sale through Jefferies LLC as the sales agent (the “*Sales Agent*”) from time to time by the Company of shares of Common Stock (the “*Sales Agreement Shares*”) having an aggregate offering price of up to \$95,573,843.36 pursuant to the Registration Statement, the Base Prospectus and the related prospectus supplement for the sale of the Sales Agreement Shares included in the Registration Statement (the Base Prospectus and such prospectus supplement, collectively, the “*Sales Agreement Prospectus*”), and that certain Open Market Sale Agreement dated as of November 3, 2021 between the Sales Agent and the Company (as amended, the “*Sales Agreement*”).

This opinion is being furnished in connection with the requirements of Item 601(b)(5) of Regulation S-K under the Act, and no opinion is expressed herein as to any matter pertaining to the contents of the Registration Statement or related applicable Prospectus or the Sales Agreement Prospectus, other than as expressly stated herein with respect to the issue of the Securities, including the issuance of the Sales Agreement Shares.

As such counsel, we have examined such matters of fact and questions of law as we have considered appropriate for purposes of this letter. With your consent, we have relied upon certificates and other assurances of officers of the Company and others as to factual matters without having independently verified such factual matters. We are opining herein as to the General Corporation Law of the State of Delaware (the “*DGCL*”), and with respect to the opinions set forth in paragraphs 3 through 5 below, the internal laws of the State of New York, and we express no opinion with respect to the applicability thereto, or the effect thereon, of the laws of any other jurisdiction or, in the case of Delaware, any other laws, or as to any matters of municipal law or the laws of any local agencies within any state.

Subject to the foregoing and the other matters set forth herein, it is our opinion that, as of the date hereof:

1. When an issuance of Common Stock has been duly authorized by all necessary corporate action of the Company, upon issuance, delivery and payment therefor in an amount not less than the par value thereof in the manner contemplated by the applicable Prospectus and by such corporate action, and in total amounts and numbers of shares that do not exceed the respective total amounts and numbers of shares (a) available under the certificate of incorporation, and (b) authorized by the board of directors in connection with the offering contemplated by the applicable Prospectus, such shares of Common Stock will be validly issued, fully paid and nonassessable. In rendering the foregoing opinion, we have assumed that the Company will comply with all applicable notice requirements regarding uncertificated shares provided in the DGCL.

2. When a series of Preferred Stock has been duly established in accordance with the terms of the Company’s Certificate of Incorporation and authorized by all necessary corporate action of the Company, upon issuance, delivery and payment therefor in an amount not less than the par value thereof in the manner contemplated by the applicable Prospectus and by such corporate action, and in total amounts and numbers of shares that do not exceed the respective total amounts and numbers of shares (a) available under the certificate of incorporation, and (b) authorized by the board of directors in connection with the offering contemplated by the applicable Prospectus, such shares of such series of Preferred Stock will be validly issued, fully paid and nonassessable. In rendering the foregoing opinion, we have assumed that the Company will comply with all applicable notice requirements regarding uncertificated shares provided in the DGCL.

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3. When the Applicable Indenture has been duly authorized, executed and delivered by all necessary corporate action of the Company, and when the specific terms of a particular series of Debt Securities have been duly established in accordance with the terms of the Applicable Indenture and authorized by all necessary corporate action of the Company, and such Debt Securities have been duly executed, authenticated, issued and delivered against payment therefor in accordance with the terms of the Applicable Indenture and in the manner contemplated by the applicable Prospectus and by such corporate action, such Debt Securities will be the legally valid and binding obligations of the Company, enforceable against the Company in accordance with their terms.

4. When the applicable warrant agreement has been duly authorized, executed and delivered by all necessary corporate action of the Company, and when the specific terms of a particular issuance of Warrants have been duly established in accordance with the terms of the applicable warrant agreement and authorized by all necessary corporate action of the Company, and such Warrants have been duly executed, authenticated, issued and delivered against payment therefor in accordance with the terms of the applicable warrant agreement and in the manner contemplated by the applicable Prospectus and by such corporate action (assuming the securities issuable upon exercise of such Warrants have been duly authorized and reserved for issuance by all necessary corporate action), such Warrants will be the legally valid and binding obligations of the Company, enforceable against the Company in accordance with their terms.

5. When the applicable unit agreement has been duly authorized, executed and delivered by all necessary corporate action of the Company, and when the specific terms of a particular issuance of Units have been duly authorized in accordance with the terms of the applicable unit agreement and authorized by all necessary corporate action of the Company, and such Units have been duly executed, authenticated, issued and delivered against payment therefor in accordance with the terms of the applicable unit agreement and in the manner contemplated by the applicable Prospectus and by such corporate action (assuming the securities issuable upon exercise of such Units have been duly authorized and reserved for issuance by all necessary corporate action), such Units will be the legally valid and binding obligations of the Company, enforceable against the Company in accordance with their terms.

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6. Upon the completion of all Corporate Proceedings (as defined below) relating to the Sales Agreement Shares, when the Sales Agreement Shares shall have been duly registered on the books of the transfer agent and registrar therefor in the name or on behalf of the purchasers, and have been issued by the Company against payment therefor (not less than par value) in accordance with the Corporate Proceedings and the terms of the Sales Agreement, the issuance and sale of the Sales Agreement Shares will have been duly authorized by all necessary corporate action of the Company, and the Sales Agreement Shares will be validly issued, fully paid and nonassessable. In rendering the foregoing opinion, we have assumed that (i) the Company will comply with all applicable notice requirements regarding uncertificated shares provided in the DGCL, (ii) upon the issuance of any of the Sales Agreement Shares, the total number of shares of Common Stock issued and outstanding will not exceed the total number of shares of Common Stock that the Company is then authorized to issue under the Company's certificate of incorporation and (iii) certain terms of the Sales Agreement Shares to be issued by the Company from time to time will be authorized and approved by the board of directors of the Company or one or more committees thereof established by the board of directors of the Company with the authority to issue and sell Sales Agreement Shares pursuant to the Sales Agreement in accordance with the DGCL, the Company's certificate of incorporation, the by-laws of the Company and certain resolutions of the board of directors of the Company and one or more committees thereof (with such approvals referred to herein as the "*Corporate Proceedings*") prior to issuance thereof.

Our opinions are subject to: (i) the effect of bankruptcy, insolvency, reorganization, preference, fraudulent transfer, moratorium or other similar laws relating to or affecting the rights and remedies of creditors; (ii) (a) the effect of general principles of equity, whether considered in a proceeding in equity or at law (including the possible unavailability of specific performance or injunctive relief), (b) concepts of materiality, reasonableness, good faith and fair dealing, and (c) the discretion of the court before which a proceeding is brought; and (iii) the invalidity under certain circumstances under law or court decisions of provisions providing for the indemnification of or contribution to a party with respect to a liability where such indemnification or contribution is contrary to public policy. We express no opinion as to (a) any provision for liquidated damages, default interest, late charges, monetary penalties, make-whole premiums or other economic remedies to the extent such provisions are deemed to constitute a penalty, (b) consents to, or restrictions upon, governing law, jurisdiction, venue, arbitration, remedies, or judicial relief, (c) waivers of rights or defenses, (d) any provision requiring the payment of attorneys' fees, where such payment is contrary to law or public policy, (e) any provision permitting, upon acceleration of any Debt Securities, collection of that portion of the stated principal amount thereof which might be determined to constitute unearned interest thereon, (f) the creation, validity, attachment, perfection, or priority of any lien or security interest, (g) advance waivers of claims, defenses, rights granted by law, or notice, opportunity for hearing, evidentiary requirements, statutes of limitation, trial by jury or at law, or other procedural rights, (h) waivers of broadly or vaguely stated rights, (i) provisions for exclusivity, election or cumulation of rights or remedies, (j) provisions authorizing or validating conclusive or discretionary determinations, (k) grants of setoff rights, (l) proxies, powers and trusts, (m) provisions prohibiting, restricting, or requiring consent to assignment or transfer of any right or property, (n) any provision to the extent it requires that a claim with respect to a security denominated in other than U.S. dollars (or a judgment in respect of such a claim) be converted into U.S. dollars at a rate of exchange at a particular date, to the extent applicable law otherwise provides, and (o) the severability, if invalid, of provisions to the foregoing effect.

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With your consent, we have assumed (a) that each of the Debt Securities, Warrants, Units and the Applicable Indenture, warrant agreements, and unit agreements governing such securities (collectively, the “*Documents*”) will be governed by the internal laws of the State of New York, (b) that each of the Documents has been or will be duly authorized, executed and delivered by the parties thereto, (c) that each of the Documents constitutes or will constitute legally valid and binding obligations of the parties thereto other than the Company, enforceable against each of them in accordance with their respective terms, and (d) that the status of each of the Documents as legally valid and binding obligations of the parties will not be affected by any (i) breaches of, or defaults under, agreements or instruments, (ii) violations of statutes, rules, regulations or court or governmental orders, or (iii) failures to obtain required consents, approvals or authorizations from, or to make required registrations, declarations or filings with, governmental authorities.

This opinion is for your benefit in connection with the Registration Statement and may be relied upon by you and by persons entitled to rely upon it pursuant to the applicable provisions of the Act. We consent to your filing this opinion as an exhibit to the Registration Statement and to the reference to our firm contained in each of the Prospectus and the Sales Agreement Prospectus under the heading “Legal Matters.” We further consent to the incorporation by reference of this letter and consent into any registration statement or post-effective amendment to the Registration Statement filed pursuant to Rule 462(b) under the Act with respect to the Securities. In giving such consent, we do not thereby admit that we are in the category of persons whose consent is required under Section 7 of the Act or the rules and regulations of the Commission thereunder.

Sincerely

/s/ Latham & Watkins LLP

Consent of Independent Registered Public Accounting Firm

We consent to the reference to our firm under the caption "Experts" in Amendment No.1 to the Registration Statement (Form S-3 No. 333-260726) and related Prospectus of Praxis Precision Medicines, Inc. for the registration of Common Stock, Preferred Stock, Debt Securities, Warrants, and Units and to the incorporation by reference therein of our reports dated February 28, 2022, with respect to the consolidated financial statements of Praxis Precision Medicines, Inc. and the effectiveness of internal control over financial reporting of Praxis Precision Medicines, Inc. included in its Annual Report (Form 10-K) for the year ended December 31, 2021, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP
Boston, Massachusetts
February 7, 2023

Calculation of Filing Fee Tables

Form S-3

(Form Type)

Praxis Precision Medicines, Inc.

(Exact Name of Registrant as Specified in its Charter)

Table 1: Newly Registered and Carry Forward Securities

	Security Type	Security Class Title	Fee Calculation or Carry Forward Rule	Amount Registered(3)	Proposed Maximum Offering Price Per Unit	Maximum Aggregate Offering Price(3)	Fee Rate	Amount of Registration Fee
Fees to Be Paid	Equity	Common Stock, \$0.0001 par value per share(1)		-	-	-	-	-
Fees to Be Paid	Equity	Preferred Stock, \$0.0001 par value per share(1)		-	-	-	-	-
Fees to Be Paid	Debt	Debt Securities		-	-	-	-	-
Fees to Be Paid	Other	Warrants		-	-	-	-	-
Fees to Be Paid	Other	Units		-	-	-	-	-
Fees to Be Paid	Unallocated (Universal Shelf)	(2)	457(o)	\$300,000,000	N/A	\$300,000,000	0.00011020	\$33,060.00
Fees Previously Paid	Equity	Common Stock, \$0.0001 par value per share	457(o)	\$95,573,843.36	N/A	\$95,573,843.36	0.0000927	\$8,859.70(4)
Total Offering Amounts						\$300,000,000(4)		\$33,060.00
Total Fees Previously Paid								\$8,859.70
Total Fee Offsets								—
Net Fee Due								\$24,200.30

(1) Includes rights to acquire Common Stock or Preferred Stock under any shareholder rights plan then in effect, if applicable under the terms of any such plan.

(2) An unspecified number of securities or aggregate principal amount, as applicable, is being registered as may from time to time be offered at unspecified prices and, in addition, an unspecified number of additional shares of Common Stock is being registered as may be issued from time to time upon conversion of any Debt Securities that are convertible into Common Stock or pursuant to any anti-dilution adjustments with respect to any such convertible Debt Securities.

- (3) Estimated solely for the purpose of calculating the registration fee. No separate consideration will be received for shares of Common Stock that are issued upon conversion of Debt Securities or Preferred Stock or upon exercise of Common Stock Warrants registered hereunder. The aggregate maximum offering price of all securities issued pursuant to this registration statement will not exceed \$300,000,000.
- (4) The \$300,000,000 of securities registered pursuant to this registration statement includes \$95,573,843.36 of Common Stock that may be issued and sold under a certain sales agreement with Jefferies LLC, or Sales Agreement. We paid a registration fee of \$11,587.50 at the time this registration statement was initially filed for \$125,000,000 of Common Stock that may be issued and sold under the Sales Agreement. As of the date of this registration statement, we have sold \$29,426,156.64 pursuant to the Sales Agreement. We are registering the offer and sale of the remaining \$95,573,843.36 that has not been sold pursuant to the Sales Agreement.