

Subject to Completion, Dated October 16, 2025

PRELIMINARY PROSPECTUS SUPPLEMENT

(To Prospectus Dated December 23, 2024)

PRAXIS PRECISION MEDICINES, INC.

Shares of Common Stock
Pre-Funded Warrants to Purchase up to **Shares of**
Common Stock

We are offering _____ shares of our common stock. Our common stock is listed on The Nasdaq Global Select Market, or Nasdaq, under the symbol "PRAX." On October 15, 2025, the last reported sale price of our common stock was \$57.35 per share. We are also offering to certain investors, in lieu of common stock, pre-funded warrants to purchase _____ shares of our common stock at a price of \$ _____ per underlying share, which equals the public offering price per share of the common stock less the \$0.0001 per share exercise price for each underlying share. The pre-funded warrants will be exercisable at any time after the date of issuance, subject to an ownership limitation. This prospectus supplement also relates to the offering of the shares of our common stock issuable upon the exercise of such pre-funded warrants.

Investing in our common stock and pre-funded warrants involves a high degree of risk. Please read "Risk Factors" beginning on page S-6 of this prospectus supplement, page 7 of the accompanying prospectus and under similar headings and in the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. There is no established public trading market for the pre-funded warrants, and we do not expect a market to develop. We do not intend to list the pre-funded warrants on Nasdaq or any other national securities exchange or nationally recognized trading system.

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

	<i>Per Share</i>	<i>Per Pre-Funded Warrant</i>	<i>Total</i>
Public offering price	\$	\$	\$
Underwriting discounts and commissions(1)	\$	\$	\$
Proceeds to Praxis Precision Medicines, Inc. before expenses	\$	\$	\$

(1) We have agreed to reimburse the underwriters for certain expenses. See "Underwriting."

We have granted the underwriters an option for a period of 30 days to purchase up to an additional _____ shares of our common stock at the public offering price, less underwriting discounts and commissions. Delivery of the shares of common stock and the pre-funded warrants is expected to be made on or about _____, 2025.

Joint Book-Running Managers

TD Cowen Piper Sandler Guggenheim Securities Truist Securities

Prospectus supplement dated _____, 2025.

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

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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 document is part of an automatic “shelf” registration statement on Form S-3ASR that we filed with the Securities and Exchange Commission, or the SEC, as a “well-known seasoned issuer” as defined in Rule 405 under the Securities Act of 1933, as amended, or the Securities Act, and is in two parts. The first part is this prospectus supplement, which describes the specific terms of this common stock and pre-funded warrants offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference herein. The second part, the accompanying prospectus, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined.

To the extent there is a conflict between the information contained in this prospectus supplement and the information contained in the accompanying prospectus or any document incorporated by reference therein filed prior to the date of this prospectus supplement, you should rely on the information in this prospectus supplement; provided that if any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference in the accompanying prospectus—the statement in the document having the later date modifies or supersedes the earlier statement.

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

We have not authorized anyone to provide any information other than that contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus supplement and the accompanying prospectus do not constitute an offer to sell, or a solicitation of an offer to purchase, the securities offered by this prospectus supplement and the accompanying prospectus in any jurisdiction to or from any person to whom or from whom it is unlawful to make such offer or solicitation of an offer in such jurisdiction. The information contained in this prospectus supplement or the accompanying prospectus, or incorporated by reference herein or therein is accurate only as of the respective dates thereof, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or of any sale of our common stock or pre-funded warrants. It is important for you to read and consider all information contained in this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein and therein, in making your investment decision. You should also read and consider the information in the documents to which we have referred you in the sections titled “Where You Can Find More Information” and “Incorporation by Reference” in this prospectus supplement and in the accompanying prospectus.

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

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 contained elsewhere in this prospectus supplement and the accompanying prospectus and in the documents we incorporate by reference. This summary does not contain all of the information you should consider before investing in our securities. You should read this entire prospectus supplement and the accompanying prospectus carefully, especially the risks of investing in our securities discussed under "Risk Factors" beginning on page S-6 of this prospectus supplement and under a similar heading in our [Annual Report on Form 10-K for the year ended December 31, 2024](#) and our most recent Quarterly Reports on Form 10-Q for the quarters ended [March 31, 2025](#) and [June 30, 2025](#), which are incorporated by reference in this prospectus supplement, along with our financial statements and notes to those financial statements and the other information incorporated by reference in this prospectus supplement and the accompanying prospectus, before making an investment decision.

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.

Recent Developments

On October 16, 2025, the Company announced positive topline results for the Phase 3 Essential3 program of ulixacaltamide in essential tremor ("ET").

About the Essential3 Program Trial Design

The Essential3 Phase 3 program (NCT06087276) included two simultaneously enrolled studies utilizing a decentralized design conducted within the United States, where participants were allocated to the studies in a 2:1 blinded randomization (Study 1:Study 2).

Study 1 was a double-blind, parallel design, placebo-controlled study that enrolled 473 patients randomized 1:1 to receive either ulixacaltamide or placebo for 12 weeks. The primary endpoint was the change from baseline in mADL11 at Week 8.

Study 2 was a stable-responder randomized withdrawal study that enrolled 238 patients to receive ulixacaltamide for 8 weeks. Patients who improved by 3 points in the mADL11 from baseline were then randomized to receive either placebo or to continue receiving ulixacaltamide for an additional 4 weeks. The primary endpoint evaluated the proportion of patients who maintained response receiving ulixacaltamide versus placebo.

There were two additional pre-specified hypotheses evaluating combinations of arms in Study 1 and Study 2 using the change in mADL11 at Week 8. Hypothesis 3 compared the ulixacaltamide arms of Study 1 and Study 2 with the placebo arm of Study 1, and Hypothesis 4 compared the ulixacaltamide arm of Study 2 with the placebo arm of Study 1.

Key secondary endpoints in Studies 1 and 2 assessed the rate of disease improvement (slope of mADL11 change), the Patient Global Impression of change (“PGI-C”) and Clinical Global Impression of severity (“CGI-S”).

Summary of Essential3 Program Results

Study 1: Placebo-controlled Parallel Group Study Topline Efficacy Results

In Study 1, there was a statistically significant and clinically meaningful 4.3 point mean improvement in the mADL11 score at Week 8 ($p < 0.0001$). The effect was sustained from Week 2 throughout the 12-week dosing period. All key secondary endpoints achieved statistical significance.

Results Summary

<u>mITT population</u>	<u>Ulixacaltamide (n=199)</u>	<u>Placebo (n=233)</u>	<u>p-value</u>
Primary Endpoint			
Day 56 CFB mADL11	-4.3	-1.7	<0.0001
Key Secondary Endpoints			
Rate of Disease Improvement, Baseline to Day 56 mADL11	-4.0	-1.7	<0.0001
PGI-C Day 56	3.3	3.9	<0.0001
CGI-S CFB to Day 56	-0.41	-0.12	0.0007
Select Sensitivity Analyses			
Imputation of missing data for primary analysis*	-3.3	-1.6	0.0026
Day 84 CFB mADL11**	-3.4	-1.9	0.0049

* Results from a pre-specified delta-adjusted tipping-point analysis remained statistically significant at the maximum tested shift ($\Delta=2.5$; $p=0.0026$), exceeding the $\sim\frac{1}{2}$ SD robustness criterion of Ratitch et al. (2013) and confirming strong resilience of the primary endpoint to non-MAR assumptions.

** Primary endpoint at the time of interim analysis (assessed as the average of Day 77 and Day 84)

Study 2: Randomized Withdrawal Study Topline Efficacy Results

In Study 2, after blinded exposure for 8 weeks with ulixacaltamide, patients meeting the responder criteria (n=80) were then randomized to continue receiving ulixacaltamide or switch to placebo for an additional 4 weeks. 55% of patients in the ulixacaltamide arm maintained response vs 33% in the placebo group ($p=0.0369$, OR=2.7 CI (1.06-6.92)). The first key secondary endpoint — rate of disease improvement — achieved statistical significance, and other secondary endpoints (PGI-C, CGI-S) were numerically in favor of ulixacaltamide, but not statistically significant.

Results Summary

<u>mITT population</u>	<u>Ulixacaltamide (n=40)</u>	<u>Placebo (n=40)</u>	<u>p-value</u>
Primary Endpoint			
Maintenance of Response	55%	33%	0.037
Key Secondary Endpoints			
Rate of Disease Improvement, RW Baseline to Day 84	2.8	5.2	0.004
PGI-C Day 84	3.24	3.67	0.087
CGI-S Day 56 to Day 84	0.39	0.73	0.055
Select Exploratory Endpoint			
PGI-S Day 56 to Day 84	0.24	0.59	0.027

Combined Study 1 and Study 2 Hypotheses

Hypothesis 3 and 4 further supported the precision of the effect of ulixacaltamide versus placebo.

- For Hypothesis 3, there was a 4.3 point improvement in mADL11 at Week 8 for the combined Studies 1 and 2 ulixacaltamide groups vs Study 1 placebo ($p < 0.0001$).

- For Hypothesis 4, there was a 4.2 point improvement in mADL11 at Week 8 for the Study 2 ulixacaltamide group vs Study 1 placebo ($p < 0.0001$), respectively.

Safety

Ulixacaltamide was generally well tolerated over 12 weeks of treatment. The most common ($\geq 10\%$ patients) treatment emergent adverse events (“TEAs”) were constipation, dizziness, euphoric mood, brain fog, headache, paraesthesia and insomnia. There were no deaths and no drug-related serious adverse events. Discontinuations were primarily due to TEAs, with the most common being dizziness and brain fog.

Overview of Adverse Events

Category	Study 1		Study 2
	Ulixacaltamide (n = 233)	Placebo (n = 234)	Ulixacaltamide (n = 231)
Participants with any TEAE	221 (94.9%)	177 (75.6%)	209 (90.5%)
Participants with:			
Mild TEAs	98 (42.0%)	89 (38.0%)	87 (37.7%)
Moderate TEAs	109 (46.8%)	78 (33.3%)	105 (45.5%)
Severe TEAs	14 (6.0%)	10 (4.3%)	17 (7.4%)
Participants with any SAE*	2 (0.86%)	8 (3.4%)	4 (1.73%)
Participants with drug-related TEAs leading to discontinuation	63 (27.0%)	4 (1.7%)	65 (28.1%)
Discontinued from the study	83 (35.6%)	13 (5.6%)	88 (38.1%)

* not related to study drug

Corporate Updates

We have submitted a pre-NDA meeting request to the FDA with plans to submit the NDA by early 2026, upon agreement with the agency.

We intend to share additional data from these studies at upcoming medical conferences and peer reviewed publications.

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
Pre-funded warrants offered by us	We are also offering, in lieu of common stock to certain investors, pre-funded warrants to purchase up to _____ shares of our common stock. The purchase price of the pre-funded warrants matches the price per share at which the shares of our common stock are being sold to the public in this offering, minus \$0.0001, which is the per share exercise price of the pre-funded warrants. The pre-funded warrants will be exercisable at any time after the date of issuance of such pre-funded warrants, subject to an ownership limitation. See “Description of Pre-funded Warrants.” This prospectus supplement also relates to the offering of the shares of our common stock issuable upon exercise of the pre-funded warrants.
Underwriters’ option	We have granted the underwriters an option to purchase up to additional shares of our common stock. This option is exercisable, in whole or in part, for a period of 30 days from the date of this prospectus supplement.
Common stock to be outstanding immediately after this offering	_____ shares (or _____ shares if the underwriters exercise in full their option to purchase additional shares), excluding shares of common stock issuable upon exercise of the pre-funded warrants.
Use of proceeds	We currently intend to use the net proceeds from this offering, together with our existing cash, cash equivalents and marketable securities, to continue our research and development activities of our clinical-stage product candidates, and preparation activities for potential commercialization of our late stage assets as well as advancement of our earlier stage assets and for working capital and other general corporate purposes. Please see “Use of Proceeds” on page S-10 .
Risk factors	Investing in our securities involves significant risks. See “Risk Factors” beginning on page S-6 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement, for a discussion of factors that you should read and consider before investing in our securities.
Nasdaq Global Select Market symbol	Our common stock is listed on The Nasdaq Global Select Market under the symbol “PRAX.” We do not intend to list the pre-funded warrants on Nasdaq or any other nationally recognized securities exchange or trading system.

The number of shares of common stock to be outstanding after this offering is based on 21,165,933 shares of common stock outstanding as of September 30, 2025 and excludes:

- 2,070,371 shares of our common stock issuable upon the exercise of stock options outstanding as of September 30, 2025 under our 2017 Stock Incentive Plan, 2020 Stock Option and Incentive Plan and 2024 Inducement Plan, at a weighted average exercise price of \$87.20 per share;
- 462,188 shares of our common stock reserved for future issuance under our 2020 Stock Option and Incentive Plan as of September 30, 2025;
- 294,552 shares of our common stock reserved for future issuance under our 2020 Employee Stock Purchase Plan as of September 30, 2025;

- 516,119 shares of our common stock reserved for future vesting of restricted stock units under our 2020 Stock Option and Incentive Plan and 2024 Inducement Plan as of September 30, 2025;
- 950,600 shares of our common stock reserved for future issuance under our 2024 Inducement Plan as of September 30, 2025;
- 925,463 shares of our common stock issuable upon the exercise of pre-funded warrants outstanding as of September 30, 2025, at an exercise price of \$0.0001 per share; and
- 197,123 shares of our common stock issued after September 30, 2025 pursuant to a Sales Agreement by and between us and TD Securities (USA) LLC, dated as of September 5, 2025.

Unless otherwise indicated, this prospectus supplement reflects and assumes the following:

- no exercise of the outstanding options and no vesting of the outstanding restricted stock units described above;
- no exercise by the underwriters of their option to purchase additional shares of our common stock; and
- no exercise of the pre-funded warrants outstanding described above or offered hereby.

RISK FACTORS

Investing in our securities 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 for the fiscal year ended December 31, 2024](#), our most recent Quarterly Reports on Form 10-Q for the quarters ended [March 31, 2025](#) and [June 30, 2025](#) and our 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 shares of 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. With aggregate gross proceeds of \$ million, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, investors in this offering would experience immediate dilution of \$ per share, representing the difference between our as adjusted net tangible book value per share as of June 30, 2025 of \$, after giving effect to this offering, and the public offering price.

In addition, we have a significant number of stock options, pre-funded warrants and restricted stock units outstanding. The exercise of any of the outstanding options or pre-funded warrants 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 or warrants, 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. 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.

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

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

We may not receive a significant amount or any additional funds upon the exercise of the pre-funded warrants.

The pre-funded warrants are exercisable for \$0.0001 per share of common stock underlying such pre-funded warrants or it may be exercised by way of a cashless exercise, meaning that the holders may not pay a cash purchase price upon exercise, but instead would receive upon such exercise the net number of shares of our common stock determined according to the formula set forth in the pre-funded warrants. Accordingly, we may not receive a significant amount or any additional funds upon the exercise of the pre-funded warrants.

The holders of the pre-funded warrants purchased in this offering will have no rights as holders of our common stock with respect to the shares of common stock underlying such pre-funded warrants until such holders exercise the pre-funded warrants and acquire our common stock.

Until a holder of our pre-funded warrants acquires shares of our common stock upon exercise of the pre-funded warrants, such holder of the pre-funded warrants will have no rights with respect to the shares of our common stock underlying such pre-funded warrants including with respect to dividends and voting rights. Upon exercise of the pre-funded warrants, such holder will be entitled to exercise the rights of a holder of our common stock with respect to the shares of common stock underlying such pre-funded warrants only as to matters for which the record date occurs after the exercise date.

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

A holder of the pre-funded warrants will not be entitled to exercise any portion of such pre-funded warrants which, upon giving effect to such exercise, would cause (i) the aggregate number of shares of our common stock beneficially owned by the holder (together with its affiliates) to exceed 4.99% (or 9.99%) of the number of shares of our common stock outstanding immediately after giving effect to the exercise, or (ii) the combined voting power of our securities beneficially owned by the holder (together with its affiliates) to exceed 4.99% (or 9.99%) of the combined voting power of all of our securities then outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the pre-funded warrants. Such percentage may be increased or decreased by the holder of the pre-funded warrants to any other percentage not in excess of 19.99% upon at least 61 days' prior notice from the holder to us.

As a result, you may not be able to exercise your pre-funded warrants for shares of our common stock at a time when it would be financially beneficial for you to do so. In such circumstance you could seek to sell your pre-funded warrants to realize value, but you may be unable to do so in the absence of an established trading market for the pre-funded warrants.

SPECIAL 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;

- our expectations regarding the completion of this offering; and
- our intended use of proceeds for this offering and the sufficiency of those proceeds with our existing cash, cash equivalents and marketable securities to fund our operations for the periods described.

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, 2024](#), our most recent Quarterly Reports on Form 10-Q for the quarters ended [March 31, 2025](#) and [June 30, 2025](#), and the section in this prospectus supplement titled “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 estimate that the net proceeds from the sale of _____ shares of our common stock and pre-funded warrants to purchase _____ shares of our common stock in this offering, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, will be approximately \$ _____ million, or approximately \$ _____ million, if the underwriters exercise their option to purchase additional shares in full. We will receive nominal proceeds, if any, upon exercise of the pre-funded warrants.

We currently intend to use the net proceeds from this offering, together with our existing cash, cash equivalents and marketable securities, to continue our research and development activities of our clinical-stage product candidates, and preparation activities for potential commercialization of our late stage assets as well as advancement of our earlier stage assets and for working capital and other general corporate purposes.

Based on the planned use of proceeds described above, we believe that the net proceeds from this offering, together with our existing cash, cash equivalents and marketable securities, will be sufficient to enable us to fund our operating expenses and capital expenditure requirements _____. We have based this estimate on assumptions that may prove to be incorrect. We could use our available capital resources sooner than we currently expect. We may satisfy our future cash needs through the sale of equity securities, debt financings, working capital lines of credit, corporate collaborations or license agreements, grant funding, interest income earned on invested cash balances or a combination of one or more of these sources.

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 June 30, 2025 was approximately \$404.2 million, or approximately \$19.21 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 June 30, 2025.

After giving effect to our issuance and sale of shares of our common stock in this offering at a public offering price of \$ per share and pre-funded warrants to purchase shares of our common stock at a public offering price of \$ (and excluding shares of common stock issued and any proceeds received upon exercise of the pre-funded warrants), and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of June 30, 2025 would have been \$ million, or \$ per share. This represents an immediate increase in as adjusted net tangible book value per share of \$ to existing stockholders and immediate dilution of \$ in as adjusted net tangible book value per share to new investors purchasing common stock in this offering. Dilution per share to new investors is determined by subtracting as adjusted net tangible book value per share after this offering from the public offering price per share paid by new investors. The following table illustrates this per share dilution to the new investors purchasing shares of common stock in this offering without giving effect to the option to purchase additional shares granted to the underwriter:

Public offering price per share	\$
Net tangible book value per share as of June 30, 2025	\$19.21
Increase in as adjusted net tangible book value per share attributable to this offering	
As adjusted net tangible book value per share after this offering	
Dilution per share to new investors participating in this offering	\$

If the underwriters exercise their option to purchase additional shares in full at the public offering price of \$ per share, the as adjusted net tangible book value will increase to \$ per share, representing an immediate increase to existing stockholders of \$ per share and an immediate dilution of \$ per share to new investors.

If holders of pre-funded warrants exercise the pre-funded warrants (and the underwriters exercise their option to purchase additional shares in full), the as adjusted net tangible book value per share of our common stock after giving effect to this offering would be \$ per share, and the dilution in net tangible book value per share to investors in this offering would be \$ per share.

The above discussion and table are based on 21,040,474 shares of common stock outstanding as of June 30, 2025 and excludes:

- 2,102,627 shares of our common stock issuable upon the exercise of stock options outstanding as of June 30, 2025 under our 2017 Stock Incentive Plan, 2020 Stock Option and Incentive Plan and 2024 Inducement Plan, at a weighted average exercise price of \$86.63 per share;
- 442,049 shares of our common stock reserved for future issuance under our 2020 Stock Option and Incentive Plan as of June 30, 2025;
- 294,552 shares of our common stock reserved for future issuance under our 2020 Employee Stock Purchase Plan as of June 30, 2025;
- 515,596 shares of our common stock issuable upon vesting of restricted stock units outstanding as of June 30, 2025 under our 2020 Stock Option and Incentive Plan and 2024 Inducement Plan;
- 962,101 shares of our common stock reserved for future issuance under our 2024 Inducement Plan as of June 30, 2025;

- 925,463 shares of our common stock issuable upon the exercise of pre-funded warrants outstanding as of June 30, 2025, at an exercise price of \$0.0001 per share; and
- 316,487 shares of our common stock issued after June 30, 2025 pursuant to a Sales Agreement by and between us and TD Securities (USA) LLC, dated as of September 5, 2025.

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, pre-funded warrants are exercised, 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.

DESCRIPTION OF PRE-FUNDED WARRANTS

The following is a brief summary of certain terms and conditions of the pre-funded warrants being offered in this offering. The following description is subject in all respects to the provisions contained in the pre-funded warrants. This prospectus supplement also relates to the offering of the shares of our common stock issuable upon exercise of the pre-funded warrants.

Form

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

Term

The pre-funded warrants will expire on the date the warrants are exercised in full.

Exercisability

The pre-funded warrants are exercisable at any time after their original issuance. The pre-funded warrants will be exercisable, at the option of each holder, in whole or in part by delivering to us a duly executed exercise notice and by payment in full of the exercise price in immediately available funds for the number of shares of common stock purchased upon such exercise. As an alternative to payment in immediately available funds, the holder may, in its sole discretion, elect to exercise the pre-funded warrants through a cashless exercise, in which the holder would receive upon such exercise the net number of shares of our common stock determined according to the formula set forth in the pre-funded warrants.

No fractional shares of our common stock will be issued in connection with the exercise of a pre-funded warrant. In lieu of fractional shares, we will pay the holder an amount in cash equal to the fractional amount multiplied by the fair market value of our common stock on the exercise date.

Exercise Limitations

We may not effect the exercise of the pre-funded warrants, and a holder will not be entitled to exercise any portion of the pre-funded warrants that, upon giving effect to such exercise, would cause: (i) the aggregate number of shares of our common stock beneficially owned by such holder (together with its affiliates) to exceed 4.99% (or 9.99%) of the number of shares of our common stock outstanding immediately after giving effect to the exercise; or (ii) the combined voting power of our securities beneficially owned by such holder (together with its affiliates) to exceed 4.99% (or 9.99%) of the combined voting power of all of our securities outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the pre-funded warrants. However, the holder of the pre-funded warrants may increase or decrease such percentage to any other percentage not in excess of 19.99% upon at least 61 days' prior notice from the holder to us.

Exercise Price

The exercise price of our common stock purchasable upon the exercise of the pre-funded warrants is \$0.0001 per share. The exercise price of the pre-funded warrants and the number of shares of our common stock issuable upon exercise of the pre-funded warrants is subject to appropriate adjustment in the event of certain stock dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting our common stock.

Transferability

Subject to applicable laws, the pre-funded warrants may be offered for sale, sold, transferred or assigned without our consent.

Exchange Listing

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

Fundamental Transactions

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

No Rights as a Stockholder

Except as otherwise set forth in the form of pre-funded warrants or, except by virtue of such holder's ownership of shares of our common stock, the holder of the pre-funded warrants does not have the rights or privileges of a holder of our common stock, including any voting rights, until such holder exercises the pre-funded warrants.

MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES

The following discussion is a summary of the material U.S. federal income tax consequences of the purchase, ownership, and disposition of our common stock and pre-funded warrants issued pursuant to this offering, but does not purport to be a complete analysis of all potential tax effects. The effects of other U.S. federal tax laws, such as estate and gift tax laws, and any applicable state, local, or foreign tax laws are not discussed. This discussion is based on the Internal Revenue Code of 1986, as amended, or the Code, Treasury Regulations promulgated thereunder, judicial decisions, and published rulings and administrative pronouncements of the Internal Revenue Service, or the IRS, in each case, as in effect as of the date of this offering. These authorities may change or be subject to differing interpretations. Any such change or differing interpretation may be applied retroactively in a manner that could adversely affect a holder of our common stock or pre-funded warrants. We have not sought and do not currently intend to seek any rulings from the IRS regarding the matters discussed below. There can be no assurance the IRS or a court will not take a contrary position to the discussion below regarding the tax consequences of the purchase, ownership, and disposition of our common stock or pre-funded warrants.

This discussion is limited to holders that hold our common stock or pre-funded warrants as “capital assets” within the meaning of Section 1221 of the Code (generally, property held for investment). This discussion does not address all U.S. federal income tax consequences relevant to a holder’s particular circumstances, including the impact of the Medicare contribution tax on net investment income and the alternative minimum tax. In addition, it does not address consequences relevant to holders subject to special rules, including, without limitation:

- U.S. expatriates and former citizens or long-term residents of the United States;
- persons holding our common stock or pre-funded warrants as part of a hedge, straddle or other risk reduction strategy, or as part of a conversion transaction or other integrated investment;
- banks, insurance companies, and other financial institutions;
- real estate investment trusts or regulated investment companies;
- brokers, dealers, or traders in securities or currencies;
- “controlled foreign corporations,” “passive foreign investment companies,” and corporations that accumulate earnings to avoid U.S. federal income tax;
- S corporations, partnerships or other entities or arrangements treated as pass-through entities for U.S. federal income tax purposes (and investors therein);
- tax-exempt organizations or governmental organizations;
- persons deemed to sell our common stock or pre-funded warrants under the constructive sale provisions of the Code;
- “qualified foreign pension funds” as defined in Section 897(l)(2) of the Code and entities all of the interests of which are held by qualified foreign pension funds;
- persons who hold or receive our common stock or pre-funded warrants pursuant to the exercise of any employee stock option or otherwise as compensation; and
- tax-qualified retirement plans.

If a partnership (or other entity or arrangement treated as a partnership for U.S. federal income tax purposes) holds our common stock or pre-funded warrants, the tax treatment of a partner in the partnership will depend on the status of the partner, the activities of the partnership, and certain determinations made at the partner level. Accordingly, partnerships holding our common stock or pre-funded warrants and the partners in such partnerships should consult their tax advisors regarding the U.S. federal income tax consequences to them.

THIS DISCUSSION IS NOT TAX ADVICE. INVESTORS SHOULD CONSULT THEIR TAX ADVISORS WITH RESPECT TO THE APPLICATION OF THE U.S. FEDERAL INCOME TAX LAWS TO THEIR PARTICULAR SITUATIONS AS WELL AS ANY TAX CONSEQUENCES OF THE PURCHASE, OWNERSHIP, AND DISPOSITION OF OUR COMMON STOCK OR PRE-FUNDED WARRANTS

ARISING UNDER THE U.S. FEDERAL ESTATE OR GIFT TAX LAWS OR UNDER THE LAWS OF ANY STATE, LOCAL, OR NON-U.S. TAXING JURISDICTION OR UNDER ANY APPLICABLE INCOME TAX TREATY.

Pre-Funded Warrants

Although it is not entirely free from doubt, a pre-funded warrant should be treated as a share of our common stock for U.S. federal income tax purposes and a holder of a pre-funded warrant should generally be taxed in the same manner as a holder of such common stock, as described below. Accordingly, no gain or loss should be recognized (other than with respect to cash paid in lieu of a fractional share) upon the exercise of a pre-funded warrant and, upon exercise, the holding period of a pre-funded warrant should carry over to the common stock received. Similarly, the tax basis of the pre-funded warrant should carry over to the common stock received upon exercise, increased by the exercise price per share of common stock.

Our characterization is not binding on the IRS, and the IRS may treat a pre-funded warrant as a warrant to acquire our common stock.

In that case, the amount and character of any gain or loss with respect to an investment in our pre-funded warrants could be materially different than the discussion set forth below. Accordingly, each prospective investor in our pre-funded warrants should consult such investor's tax advisor regarding the risks associated with the purchase, ownership, and disposition of pre-funded warrants pursuant to this offering (including potential alternative characterizations). The remainder of this discussion generally assumes that a pre-funded warrant is treated as a share of our common stock for U.S. federal income tax purposes.

Tax Considerations Applicable to U.S. Holders

Definition of a U.S. Holder

For purposes of this discussion, a "U.S. holder" is a beneficial owner of our common stock or the pre-funded warrants that, for U.S. federal income tax purposes, is or is treated as any of the following:

- an individual who is a citizen or resident of the United States;
- a corporation created or organized under the laws of the United States, any state thereof, or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income tax regardless of its source; or
- a trust that (1) is subject to the primary supervision of a U.S. court and one or more "United States persons" (within the meaning of Section 7701(a)(30) of the Code) have the authority to control all substantial decisions of the trust or (2) has a valid election in effect to be treated as a United States person for U.S. federal income tax purposes.

Distributions

As described in the section titled "Dividend Policy," we do not intend to pay cash dividends to our stockholders in the foreseeable future. However, if we do make distributions of cash or property on our common stock or pre-funded warrants, such distributions will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Dividends received by a corporate U.S. holder may be eligible for a dividends received deduction, subject to applicable limitations. Dividends received by certain non-corporate U.S. holders, including individuals, are generally taxed at the lower applicable capital gains rate provided certain holding period and other requirements are satisfied.

Amounts not treated as dividends for U.S. federal income tax purposes will constitute a return of capital and first be applied against and reduce a U.S. holder's adjusted tax basis in our common stock or pre-funded warrants, but not below zero. Any excess will be treated as capital gain and will be treated as described below under "*—Tax Considerations Applicable to U.S. Holders—Sale or Other Taxable Disposition.*"

Constructive Distributions on Pre-Funded Warrants

A U.S. holder of pre-funded warrants may, in some circumstances, be deemed to have received a distribution subject to U.S. federal income tax as a result of an adjustment or the non-occurrence of an

adjustment to the exercise price or number of shares of common stock issuable upon exercise of such pre-funded warrants. U.S. holders should consult their tax advisors regarding the proper treatment of any adjustments or the non-occurrence of an adjustment to pre-funded warrants.

Sale or Other Taxable Disposition

Upon the sale, exchange, or other taxable disposition of the common stock or pre-funded warrants, a U.S. holder generally will recognize capital gain or loss equal to the difference between (i) the amount of cash and the fair market value of any property received upon the sale, exchange or other taxable disposition and (ii) such U.S. holder's adjusted tax basis in the common stock or pre-funded warrants. Such capital gain or loss will be long term capital gain or loss if the U.S. holder's holding period in such common stock or pre-funded warrants is more than one year at the time of the sale, exchange or other taxable disposition. Long-term capital gains recognized by certain non-corporate U.S. holders, including individuals, generally will be subject to reduced rates of U.S. federal income tax. The deductibility of capital losses is subject to certain limitations.

Information Reporting and Backup Withholding

A U.S. holder may be subject to information reporting and backup withholding if such holder receives distributions on the common stock or pre-funded warrants (including constructive distributions) or receives proceeds from the sale or other taxable disposition of common stock or pre-funded warrants. Certain U.S. holders are exempt from backup withholding. A U.S. holder will be subject to backup withholding if such holder is not otherwise exempt and such holder:

- fails to furnish the holder's taxpayer identification number, which for an individual is ordinarily such individual's social security number;
- furnishes an incorrect taxpayer identification number;
- is notified by the IRS that the holder previously failed to properly report payments of interest or dividends; or
- fails to certify under penalties of perjury that the holder has furnished a correct taxpayer identification number and that the IRS has not notified the holder that the holder is subject to backup withholding.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against a U.S. holder's U.S. federal income tax liability, provided the required information is timely furnished to the IRS. U.S. holders should consult their tax advisors regarding their qualification for an exemption from backup withholding and the procedures for obtaining such an exemption.

Tax Considerations Applicable to Non-U.S. Holders

Definition of a Non-U.S. Holder

For purposes of this discussion, a "non-U.S. holder" is a beneficial owner of our common stock or pre-funded warrants that is neither a U.S. holder nor an entity treated as a partnership for U.S. federal income tax purposes.

Distributions

As described in the section titled "Dividend Policy," we do not intend to pay cash dividends to our stockholders in the foreseeable future. However, if we do make distributions of cash or property on our common stock or pre-funded warrants, such distributions will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles.

Amounts not treated as dividends for U.S. federal income tax purposes will constitute a return of capital and first be applied against and reduce a non-U.S. holder's adjusted tax basis in our common stock or pre-funded warrants, but not below zero. Any excess will be treated as capital gain and will be treated as described below under "*Tax Considerations Applicable to Non-U.S. Holders—Sale or Other Taxable Disposition.*" Because we may not know the extent to which a distribution is a dividend for U.S. federal income tax purposes at the time it is made, for purposes of the withholding rules discussed below, we or the applicable withholding agent may treat the entire distribution as a dividend.

Subject to the discussion below on effectively connected income, dividends paid to a non-U.S. holder will be subject to U.S. federal withholding tax at a rate of 30% of the gross amount of the dividends (or such lower rate specified by an applicable income tax treaty, provided the non-U.S. holder furnishes a valid IRS Form W-8BEN or W-8BEN-E (or other applicable documentation) certifying qualification for such lower rate under an income tax treaty between the United States and the country in which the non-U.S. holder resides or is established). This certification must be provided to the applicable withholding agent prior to the payment of dividends and must be updated periodically. A non-U.S. holder that does not timely furnish the required documentation, but that qualifies for a reduced treaty rate, may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS. Non-U.S. holders should consult their tax advisors regarding their entitlement to benefits under any applicable tax treaties that may provide for different rules.

If dividends paid to a non-U.S. holder are effectively connected with the non-U.S. holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the non-U.S. holder maintains a permanent establishment in the United States to which such dividends are attributable), then the non-U.S. holder will be exempt from the U.S. federal withholding tax described above. To claim the exemption, the non-U.S. holder must furnish to the applicable withholding agent a valid IRS Form W-8ECI, certifying that the dividends are effectively connected with the non-U.S. holder's conduct of a trade or business within the United States. This certification must be provided to the applicable withholding agent prior to the payment of dividends and must be updated periodically. Any such effectively connected dividends will be subject to U.S. federal income tax on a net income basis at the regular rates. In addition, a non-U.S. holder that is a corporation may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on its effectively connected dividends, as adjusted for certain items. Non-U.S. holders should consult their tax advisors regarding their entitlement to benefits under any applicable income tax treaty.

Constructive Distributions on Pre-Funded Warrants

A non-U.S. holder of pre-funded warrants may be treated as receiving deemed payment of a taxable dividend as a result of an adjustment or the non-occurrence of an adjustment to the exercise price or number of shares of common stock issuable upon exercise of such pre-funded warrants. Non-U.S. holders should consult their tax advisors regarding the proper treatment of any adjustments or the non-occurrence of an adjustment to the pre-funded warrants.

Sale or Other Taxable Disposition

A non-U.S. holder will not be subject to U.S. federal income tax on any gain realized upon the sale or other taxable disposition of our common stock or pre-funded warrants unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the non-U.S. holder maintains a permanent establishment in the United States to which such gain is attributable);
- the non-U.S. holder is a nonresident alien individual present in the United States for 183 days or more during the taxable year of the disposition (as calculated pursuant to Section 7701(b) of the Code) and certain other requirements are met; or
- our common stock or pre-funded warrants constitute a U.S. real property interest, or USRPI, by reason of our status as a U.S. real property holding corporation, or USRPHC, for U.S. federal income tax purposes.

Gain described in the first bullet point above will generally be subject to U.S. federal income tax on a net income basis at the regular rates. A non-U.S. holder that is a corporation also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on such effectively connected gain, as adjusted for certain items.

A non-U.S. holder described in the second bullet point above will be subject to U.S. federal income tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on any gain realized upon the sale or other taxable disposition of our common stock or pre-funded warrants, which may be offset by U.S. source capital losses of the non-U.S. holder (even though the individual is not considered a resident of the United States), provided the non-U.S. holder has timely filed U.S. federal income tax returns with respect to such losses.

With respect to the third bullet point above, we believe we currently are not, and do not anticipate becoming, a USRPHC. Because the determination of whether we are a USRPHC depends, however, on the fair market value of our USRPIs relative to the fair market value of our other business assets and our non-U.S. real property interests, there can be no assurance we currently are not a USRPHC or will not become one in the future. Even if we are or were to become a USRPHC, gain arising from the sale or other taxable disposition of our common stock or pre-funded warrants by a non-U.S. holder will not be subject to U.S. federal income tax if our common stock or pre-funded warrants are treated as “regularly traded,” as defined by applicable Treasury Regulations, on an established securities market, and such non-U.S. holder owned, actually and constructively, 5% or less of our common stock and/or pre-funded warrants throughout the shorter of the five-year period ending on the date of the sale or other taxable disposition or the non-U.S. holder’s holding period for such common stock or pre-funded warrants.

Non-U.S. holders should consult their tax advisors regarding potentially applicable income tax treaties that may provide for different rules.

Information Reporting and Backup Withholding

Payments of dividends on our common stock or pre-funded warrants to a non-U.S. holder will not be subject to backup withholding, provided the applicable withholding agent does not have actual knowledge or reason to know the holder is a United States person and the holder either certifies its non-U.S. status, such as by furnishing a valid IRS Form W-8BEN, W-8BEN-E, or W-8ECI, or otherwise establishes an exemption. However, information returns are required to be filed with the IRS in connection with any distributions on our common stock or pre-funded warrants paid to the non-U.S. holder, regardless of whether such distributions constitute dividends or whether any tax was actually withheld. In addition, proceeds of the sale or other taxable disposition of our common stock or pre-funded warrants within the United States or conducted through certain U.S.-related brokers generally will not be subject to backup withholding or information reporting if the applicable withholding agent receives the certification described above and does not have actual knowledge or reason to know that such holder is a United States person or the holder otherwise establishes an exemption. Proceeds of a disposition of our common stock or pre-funded warrants conducted through a non-U.S. office of a non-U.S. broker generally will not be subject to backup withholding or information reporting.

Copies of information returns that are filed with the IRS may also be made available under the provisions of an applicable treaty or agreement to the tax authorities of the country in which the non-U.S. holder resides or is established.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against a non-U.S. holder’s U.S. federal income tax liability, provided the required information is timely furnished to the IRS.

Additional Withholding Tax on Payments Made to Foreign Accounts

Withholding taxes may be imposed under Sections 1471 to 1474 of the Code (such Sections commonly referred to as the Foreign Account Tax Compliance Act, or FATCA) on certain types of payments made to non-U.S. financial institutions and certain other non-U.S. entities. Specifically, a 30% withholding tax may be imposed on dividends (including deemed dividends) on, or (subject to the proposed Treasury Regulations discussed below) gross proceeds from the sale or other disposition of, our common stock or pre-funded warrants paid to a “foreign financial institution” or a “non-financial foreign entity” (each as defined in the Code), unless (1) the foreign financial institution undertakes certain diligence and reporting obligations, (2) the non-financial foreign entity either certifies it does not have any “substantial United States owners” (as defined in the Code) or furnishes identifying information regarding each substantial United States owner, or (3) the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from these rules. If the payee is a foreign financial institution and is subject to the diligence and reporting requirements in clause (1) above, it must enter into an agreement with the U.S. Department of the Treasury requiring, among other things, that it undertake to identify accounts held by certain “specified United States persons” or “United States owned foreign entities” (each as defined in the Code), annually report certain information about such accounts, and withhold 30% on certain payments to non-compliant foreign financial institutions and certain other account holders. Foreign financial institutions located in jurisdictions that have an intergovernmental agreement with the United States governing FATCA may be subject to different rules.

Under the applicable Treasury Regulations and administrative guidance, withholding under FATCA generally applies to payments of dividends (including deemed dividends) on our common stock or pre-funded warrants. While withholding under FATCA would have applied also to payments of gross proceeds from the sale or other disposition of stock on or after January 1, 2019, proposed Treasury Regulations eliminate FATCA withholding on payments of gross proceeds entirely. Taxpayers generally may rely on these proposed Treasury Regulations until final Treasury Regulations are issued. Because we may not know the extent to which a distribution is a dividend for U.S. federal income tax purposes at the time it is made, for purposes of these withholding rules, we or the applicable withholding agent may treat the entire distribution as a dividend.

Prospective investors should consult their tax advisors regarding the potential application of withholding under FATCA to their investment in our common stock or pre-funded warrants.

THIS DISCUSSION IS NOT TAX ADVICE. INVESTORS SHOULD CONSULT THEIR TAX ADVISORS WITH RESPECT TO THE APPLICATION OF THE U.S. FEDERAL INCOME TAX LAWS TO THEIR PARTICULAR SITUATIONS AS WELL AS ANY TAX CONSEQUENCES OF THE PURCHASE, OWNERSHIP, AND DISPOSITION OF OUR COMMON STOCK OR PRE-FUNDED WARRANTS ARISING UNDER THE U.S. FEDERAL ESTATE OR GIFT TAX LAWS OR UNDER THE LAWS OF ANY STATE, LOCAL, OR NON-U.S. TAXING JURISDICTION OR UNDER ANY APPLICABLE INCOME TAX TREATY.

UNDERWRITING

We and the underwriters for the offering named below have entered into an underwriting agreement with respect to the common stock and pre-funded warrants being offered. Subject to the terms and conditions of the underwriting agreement, each underwriter has severally agreed to purchase from us the number of shares of our common stock and pre-funded warrants set forth opposite its name below. TD Securities (USA) LLC, Piper Sandler & Co., and Guggenheim Securities, LLC are the representatives of the underwriters.

Underwriter	Number of Shares	Number of Pre-Funded Warrants
TD Securities (USA) LLC		
Piper Sandler & Co.		
Guggenheim Securities, LLC		
Truist Securities, Inc.		
Total		

The underwriting agreement provides that the obligations of the underwriters are subject to certain conditions precedent and that the underwriters have agreed, severally and not jointly, to purchase all of the shares of our common stock and pre-funded warrants sold under the underwriting agreement if any of these shares and pre-funded warrants are purchased, other than those shares covered by the option to purchase additional shares described below. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against specified liabilities, including liabilities under the Securities Act and to contribute to payments the underwriters may be required to make in respect thereof.

The underwriters are offering the shares of our common stock and pre-funded warrants, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel and other conditions specified in the underwriting agreement. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Option to Purchase Additional Shares. We have granted to the underwriters an option to purchase up to additional shares of our common stock at the public offering price, less the underwriting discounts and commissions. This option is exercisable for a period of 30 days. To the extent that the underwriters exercise this option, the underwriters will purchase additional shares from us in approximately the same proportion as shown in the table above.

Discounts and Commissions. The following table shows the public offering price, underwriting discounts and commissions and proceeds, before expenses to us. These amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

We estimate that the total expenses of the offering, excluding underwriting discounts and commissions, will be approximately \$ and are payable by us. We have agreed to reimburse the underwriters for certain expenses incurred by them in connection with the offering, in an amount not to exceed \$150,000, and up to \$15,000 for their FINRA counsel fee. In accordance with FINRA Rule 5110, this reimbursed fee is deemed underwriting compensation for this offering.

	Total		
	Per Share	Per Pre-Funded Warrant	Without Option With Option
Public offering price			
Underwriting discounts and commissions			
Proceeds, before expenses, to Praxis Precision Medicines, Inc			

The underwriters propose to offer the shares of our common stock and pre-funded warrants to the public at the public offering price set forth on the cover of this prospectus supplement. The underwriters may offer the shares of our common stock and pre-funded warrants to securities dealers at the public offering price less a concession not in excess of \$ _____ per share and \$ _____ per pre-funded warrant. If all of the shares and pre-funded warrants are not sold at the public offering price, the underwriters may change the offering price and other selling terms. Sales of any shares of common stock and pre-funded warrants may be made by affiliates of the underwriters.

Discretionary Accounts. The underwriters do not intend to confirm sales of the shares of our common stock and pre-funded warrants to any accounts over which they have discretionary authority.

Market Information. Our common stock is listed on Nasdaq under the symbol "PRAX". We do not intend to list the pre-funded warrants on Nasdaq or any other national securities exchange or nationally recognized trading system.

Stabilization. In connection with this offering, the underwriters (and their affiliates) may engage in stabilizing transactions, over-allotment transactions, syndicate covering transactions, penalty bids and purchases to cover positions created by short sales.

- Stabilizing transactions permit bids to purchase shares of common stock so long as the stabilizing bids do not exceed a specified maximum, and are engaged in for the purpose of preventing or retarding a decline in the market price of the common stock while the offering is in progress.
- Over-allotment transactions involve sales by the underwriters of shares of common stock in excess of the number of shares the underwriters are obligated to purchase. This creates a syndicate short position which may be either a covered short position or a naked short position. In a covered short position, the number of shares over-allotted by the underwriters is not greater than the number of shares that they may purchase in the option to purchase additional shares. In a naked short position, the number of shares involved is greater than the number of shares in the option to purchase additional shares. The underwriters may close out any short position by exercising their option to purchase additional shares and/or purchasing shares in the open market.
- Syndicate covering transactions involve purchases of common stock in the open market after the distribution has been completed in order to cover syndicate short positions. In determining the source of shares to close out the short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared with the price at which they may purchase shares through exercise of the option to purchase additional shares. If the underwriters sell more shares than could be covered by exercise of the option to purchase additional shares and, therefore, have a naked short position, the position can be closed out only by buying shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that after pricing there could be downward pressure on the price of the shares in the open market that could adversely affect investors who purchase in the offering.
- Penalty bids permit the representatives to reclaim a selling concession from a syndicate member when the common stock originally sold by that syndicate member is purchased in stabilizing or syndicate covering transactions to cover syndicate short positions.

These stabilizing transactions, syndicate covering transactions and penalty bids may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock in the open market may be higher than it would otherwise be in the absence of these transactions. Neither we nor the underwriters make any representation or prediction as to the effect that the transactions described above may have on the price of our common stock. These transactions may be effected on the Nasdaq Stock Market, in the over-the-counter market or otherwise and, if commenced, may be discontinued at any time.

Passive Market Making. In connection with this offering, underwriters (and their affiliates) and selling group members may engage in passive market making transactions in our common stock on the Nasdaq Stock Market in accordance with Rule 103 of Regulation M under the Exchange Act during a period before the commencement of offers or sales of common stock and extending through the completion of the distribution. A passive market maker must display its bid at a price not in excess of

the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, such bid must then be lowered when specified purchase limits are exceeded.

Lock-Up Agreements. Pursuant to the underwriting agreement and certain "lock-up" agreements, we, our executive officers and our directors have agreed, subject to specified exceptions, not to directly or indirectly:

- sell, offer, contract or grant any option to sell (including any short sale), pledge, transfer, establish an open "put equivalent position" within the meaning of Rule 16a-1(h) under Exchange Act, or
- otherwise dispose of any shares of common stock, options or warrants to acquire shares of common stock, or securities exchangeable or exercisable for or convertible into shares of common stock currently or hereafter owned either of record or beneficially, or
- publicly announce an intention to do any of the foregoing for a period of 30 days after the date of this prospectus supplement without the prior written consent of TD Securities (USA) LLC and Piper Sandler & Co.

This restriction terminates after the close of trading of the common stock on and including the 30th day after the date of this prospectus supplement (the "Lock-Up Period"). The lock-up restrictions will not apply to issuance of common stock upon the exercise of the pre-funded warrants during the Lock-Up Period.

TD Securities (USA) LLC and Piper Sandler & Co. may, in their sole discretion and at any time or from time to time before the termination of the Lock-Up Period release all or any portion of the securities subject to lock-up agreements. Except for certain lock-up exceptions, there are no existing agreements between the underwriters and us and any of our stockholders who will execute a lock-up agreement, providing consent to the sale of shares prior to the expiration of the Lock-Up Period.

Selling Restrictions

Canada. The common stock and pre-funded warrants may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 *Prospectus Exemptions* or subsection 73.3(1) of the *Securities Act* (Ontario), and are permitted clients, as defined in National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*. Any resale of the common stock and pre-funded warrants must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

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

Pursuant to section 3A.3 of National Instrument 33-105 *Underwriting Conflicts* (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Switzerland. The securities will not be offered, directly or indirectly, to the public in Switzerland and this prospectus does not constitute a public offering prospectus as that term is understood pursuant to article 652a or 1156 of the Swiss Federal Code of Obligations.

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

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

provided that no such offer of the shares of our common stock or pre-funded warrants shall require us or any of the representatives to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation.

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

United Kingdom. No shares of our common stock or pre-funded warrants have been offered or will be offered pursuant to the offering to the public in the United Kingdom prior to the publication of a prospectus in relation to the securities which has been approved by the Financial Conduct Authority, except that the shares of our common stock or pre-funded warrants may be offered to the public in the United Kingdom at any time:

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

provided that no such offer of the shares of our common stock or pre-funded warrants shall require the Issuer or any Manager to publish a prospectus pursuant to Section 85 of the FSMA or supplement a prospectus pursuant to Article 23 of the UK Prospectus Regulation. For the purposes of this provision, the expression an “offer to the public” in relation to the securities in the United Kingdom means the communication in any form and by any means of sufficient information on the terms of the offer and any shares of our common stock or pre-funded warrants to be offered so as to enable an investor to decide to purchase or subscribe for any shares of our common stock or pre-funded warrants and the expression “UK Prospectus Regulation” means Regulation (EU) 2017/1129 as it forms part of domestic law by virtue of the European Union (Withdrawal) Act 2018.

Hong Kong. The shares of our common stock or pre-funded warrants have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to “professional investors” as defined in the Securities and Futures Ordinance (Cap. 571 of the Laws of Hong Kong) (the “SFO”) of Hong Kong and any rules made thereunder; or (b) in other circumstances which do not result in the document being a “prospectus” as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32) of Hong Kong) (the “CO”), or which do not constitute an offer to the public within the meaning of the CO. No advertisement, invitation or document relating to the shares of our common stock or pre-funded warrants has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to shares of our common stock or pre-funded warrants which are or are intended to be disposed of only to persons outside Hong Kong or only to “professional investors” as defined in the SFO and any rules made thereunder.

Singapore. Each underwriter has acknowledged that this prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, each underwriter has represented

and agreed that it has not offered or sold any securities or caused the securities to be made the subject of an invitation for subscription or purchase and will not offer or sell any shares of our common stock or pre-funded warrants or cause the securities to be made the subject of an invitation for subscription or purchase, and has not circulated or distributed, nor will it circulate or distribute, this prospectus or any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the securities, whether directly or indirectly, to any person in Singapore other than:

- A. to an institutional investor (as defined in Section 4A of the Securities and Futures Act (Chapter 289) of Singapore, as modified or amended from time to time (the “SFA”)) pursuant to Section 274 of the SFA;
- B. to a relevant person (as defined in Section 275(2) of the SFA) pursuant to Section 275(1) of the SFA, or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275 of the SFA; or
- C. otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares of our common stock or pre-funded warrants are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- A. a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- B. a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor, securities or securities-based derivatives contracts (each term as defined in Section 2(1) of the SFA) of that corporation or the beneficiaries’ rights and interest (however described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the securities pursuant to an offer made under Section 275 of the SFA except:
 - (i) to an institutional investor or to a relevant person, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;
 - (ii) where no consideration is or will be given for the transfer;
 - (iii) where the transfer is by operation of law;
 - (iv) as specified in Section 276(7) of the SFA; or
 - (v) as specified in Regulation 37A of the Securities and Futures (Offers of Investments) (Securities and Securities-based Derivatives Contracts) Regulations 2018.

Singapore SFA Product Classification—In connection with Section 309B of the SFA and the CMP Regulations 2018, unless otherwise specified before an offer of securities, we have determined, and hereby notify all relevant persons (as defined in Section 309A(1) of the SFA), that the securities are “prescribed capital markets products” (as defined in the CMP Regulations 2018) and Excluded Investment Products (as defined in MAS Notice SFA 04-N12: Notice on the Sale of Investment Products and MAS Notice FAA-N16: Notice on Recommendations on Investment Products).

Israel. In the State of Israel this prospectus supplement shall not be regarded as an offer to the public to purchase shares of our common stock of our common stock or pre-funded warrants under the Israeli Securities Law, 5728—1968, which requires a prospectus to be published and authorized by the Israel Securities Authority, if it complies with certain provisions of Section 15 of the Israeli Securities Law, 5728—1968, including, inter alia, if: (i) the offer is made, distributed or directed to not more than 35 investors, subject to certain conditions (the “Addressed Investors”); or (ii) the offer is made, distributed or directed to certain qualified investors defined in the First Addendum of the Israeli Securities Law, 5728—1968, subject to certain conditions (the “Qualified Investors”). The Qualified Investors shall not be taken into account in the count of the Addressed Investors and may be offered to purchase securities

in addition to the 35 Addressed Investors. The company has not and will not take any action that would require it to publish a prospectus in accordance with and subject to the Israeli Securities Law, 5728—1968. We have not and will not distribute this prospectus or make, distribute or direct an offer to subscribe for our common stock to any person within the State of Israel, other than to Qualified Investors and up to 35 Addressed Investors.

Qualified Investors may have to submit written evidence that they meet the definitions set out in of the First Addendum to the Israeli Securities Law, 5728—1968. In particular, we may request, as a condition to be offered common stock, that Qualified Investors will each represent, warrant and certify to us and/or to anyone acting on our behalf: (i) that it is an investor falling within one of the categories listed in the First Addendum to the Israeli Securities Law, 5728—1968; (ii) which of the categories listed in the First Addendum to the Israeli Securities Law, 5728—1968 regarding Qualified Investors is applicable to it; (iii) that it will abide by all provisions set forth in the Israeli Securities Law, 5728—1968 and the regulations promulgated thereunder in connection with the offer to be issued common stock; (iv) that the securities that it will be issued are, subject to exemptions available under the Israeli Securities Law, 5728—1968: (a) for its own account; (b) for investment purposes only; and (c) not issued with a view to resale within the State of Israel, other than in accordance with the provisions of the Israeli Securities Law, 5728—1968; and (v) that it is willing to provide further evidence of its Qualified Investor status. Addressed Investors may have to submit written evidence in respect of their identity and may have to sign and submit a declaration containing, inter alia, the Addressed Investor's name, address and passport number or Israeli identification number.

We have not authorized and do not authorize the making of any offer of securities through any financial intermediary on our behalf, other than offers made by the underwriters and their respective affiliates, with a view to the final placement of the securities as contemplated in this document. Accordingly, no purchaser of the securities, other than the underwriters, is authorized to make any further offer of securities on our behalf or on behalf of the underwriters.

Electronic Offer, Sale and Distribution of Securities. A prospectus in electronic format may be made available on the websites maintained by one or more of the underwriters or selling group members, if any, participating in this offering and one or more of the underwriters participating in this offering may distribute prospectuses electronically. The representatives may agree to allocate a number of shares of our common stock and pre-funded warrants to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the underwriters and selling group members that will make internet distributions on the same basis as other allocations. Other than the prospectus in electronic format, the information on these websites is not part of this prospectus or the registration statement of which this prospectus forms a part, has not been approved or endorsed by us or any underwriter in its capacity as underwriter, and should not be relied upon by investors.

Other Relationships. Certain of the underwriters and their affiliates have provided, and may in the future provide, various investment banking, commercial banking and other financial services for us and our affiliates for which they have received, and may in the future receive, customary fees.

LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon for us by Latham & Watkins LLP. Mintz, Levin, Cohn, Ferris, Glovsky & Popeo, P.C. is counsel to the underwriters in connection with this offering.

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, 2024](#), and the effectiveness of Praxis Precision Medicines, Inc.'s internal control over financial reporting as of December 31, 2024 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 consolidated financial statements are incorporated herein by reference in reliance upon such reports given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION; INCORPORATION BY REFERENCE

Available Information

This prospectus supplement is part of an automatic “shelf” registration statement on Form S-3ASR that we have filed with the SEC as a “well-known seasoned issuer” as defined in Rule 405 under the Securities Act. 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’s rules allow us to “incorporate by reference” information into this prospectus supplement and the accompanying 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 supplement and the accompanying prospectus, and subsequent information that we file with the SEC will automatically update and supersede that information. Any statement contained in a previously filed document incorporated by reference will be deemed to be modified or superseded for purposes of this prospectus supplement and the accompanying prospectus to the extent that a statement contained in this prospectus supplement or the accompanying prospectus modifies or replaces that statement.

We incorporate by reference the following information or documents that we have filed with the SEC:

- [our Annual Report on Form 10-K for the year ended December 31, 2024, filed with the SEC on February 28, 2025;](#)
- The information specifically incorporated by reference into our [Annual Report on Form 10-K for the year ended December 31, 2024](#) from our [Definitive Proxy Statement on Schedule 14A, filed with the SEC on April 30, 2025;](#)
- our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2025 and June 30, 2025, filed with the SEC on [May 2, 2025](#) and [August 4, 2025](#), respectively;
- our Current Reports on Form 8-K filed with the SEC on [May 2, 2025](#) (Item 8.01 only), [June 27, 2025](#), [July 17, 2025](#) (Item 8.01 only), [August 4, 2025](#) (Item 8.01 only), [September 5, 2025](#) and [October 16, 2025](#) (Item 8.01 only); and
- the description of our common stock contained in our Registration Statement on [Form 8-A filed with the SEC on October 14, 2020](#), as updated by “Description of the Registrant’s Securities registered pursuant to Section 12 of the Securities Exchange Act of 1934” filed as [Exhibit 4.3](#) to our

Annual Report on Form 10-K for the fiscal year ended December 31, 2022, and any amendment or report filed for the purposes of updating this description.

We incorporate by reference into this prospectus supplement and accompanying prospectus all reports and other documents we subsequently file with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, between the date of this prospectus supplement and the termination of the offering of the securities described in this prospectus supplement. We are not, however, incorporating by reference any documents or portions thereof, whether specifically listed above or filed in the future, that are not deemed “filed” with the SEC, including any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K or related exhibits furnished pursuant to Item 9.01 of Form 8-K. The reports and documents specifically listed above or filed in the future (excluding any information furnished to, rather than filed with, the SEC) are deemed to be part of this prospectus supplement and accompanying 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 supplement (other than exhibits, unless they are specifically incorporated by reference in the documents) 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

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

PROSPECTUS

**PRAXIS PRECISION MEDICINES, INC.****Common Stock
Preferred Stock
Debt Securities
Warrants
Units**

We may offer and sell 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" BEGINNING 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 December 19, 2024, the last reported sale price of our common stock on The Nasdaq Global Select Market was \$72.84 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 December 23, 2024.

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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, as a “well-known seasoned issuer” as defined in Rule 405 under the Securities Act of 1933, as amended, or the Securities Act, 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 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 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, 2023 and any subsequent Quarterly Reports on Form 10-Q or 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 (other than any information therein furnished to, rather than filed with, the SEC):

- [our Annual Report on Form 10-K for the year ended December 31, 2023, filed with the SEC on March 5, 2024](#);
- our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2024, June 30, 2024 and September 30, 2024, filed with the SEC on [May 13, 2024](#), [August 13, 2024](#) and [November 6, 2024](#), respectively;
- our Current Reports on Form 8-K filed with the SEC on [January 10, 2024](#) (Items 3.02 and 8.01 only), [January 11, 2024](#), [January 12, 2024](#), [March 5, 2024](#) (Item 8.01 only), [March 26, 2024](#), [March 29, 2024](#), [May 13, 2024](#) (Item 8.01 only), [June 6, 2024](#), [September 3, 2024](#) (Item 8.01 only) and [October 16, 2025](#) (Item 8.01 only); and
- the description of our Common Stock contained in 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, and you should not consider any information on, or that can be accessed through, our website as part of this prospectus.

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 of 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 OTHER SECURITIES

We will set forth in the applicable prospectus supplement a description of any warrants or units issued by us that may be offered and sold pursuant to this prospectus.

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 offered securities from time to time:

- through underwriters or dealers;
- through agents;
- directly to one or more purchasers; or
- through a combination of any of these methods of sale.

We will identify the specific plan of distribution, including any underwriters, dealers, agents or direct purchasers and their compensation in the applicable prospectus supplement.

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, 2023](#), have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon included therein, and incorporated herein by reference. Such financial statements are, and audited financial statements to be included in subsequently filed documents will be, incorporated herein in reliance upon the report of Ernst & Young LLP pertaining to such financial statements (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.

PRAXIS PRECISION MEDICINES, INC.

Pre-Funded Warrants to Purchase up to
Shares of Common Stock
Shares of Common Stock
Shares of



PROSPECTUS SUPPLEMENT

Joint Book-Running Managers

TD Cowen Piper Sandler Guggenheim Securities Truist Securities

, 2025
