

Prospectus

Applied Therapeutics, Inc.



\$300,000,000
Common Stock
Preferred Stock
Depositary Shares
Debt Securities
Warrants

Offered by Applied Therapeutics, Inc.

Up to 38,250,000 Shares of Common Stock Issuable upon Exercise of Warrants

Up to 31,735,731 Shares of Common Stock for Resale
Offered by the Selling Stockholders

We may offer, issue and sell, together or separately:

- shares of our common stock;
- shares of our preferred stock, which may be issued in one or more series;
- depositary receipts, representing fractional shares of our preferred stock, which are called depositary shares;
- debt securities, which may be issued in one or more series and which may be senior debt securities or subordinated debt securities; and
- warrants to purchase shares of our common stock, shares of our preferred stock or our debt securities.

We will provide the specific prices and terms of these securities in one or more supplements to this prospectus at the time of offering. You should read this prospectus and the accompanying prospectus supplement carefully before you make your investment decision. The aggregate offering price of all securities that may be sold by us, excluding the shares issuable by us upon exercise of the 2022 Warrants (as defined below), under this prospectus will not exceed \$300,000,000.

In addition, this prospectus relates to the issuance by us of up to 38,250,000 shares of our common stock, par value \$0.0001 per share, that are issuable upon the exercise of (i) 8,250,000 outstanding pre-funded warrants, with an exercise price of \$0.001 per warrant (the “2022 Pre-Funded Warrants”), and (ii) 30,000,000 outstanding common warrants, with an exercise price of \$1.00 per warrant (the “2022 Common Warrants” and together with the 2022 Pre-Funded Warrants the “2022 Warrants”), that we previously issued in a public offering pursuant to registration statement on Form S-3 on June 22, 2022.

This prospectus also relates to the offer and sale from time to time by the selling stockholders identified in this prospectus of up to 31,735,731 shares of common stock, of which 22,000,000 shares are issuable upon the exercise of pre-funded warrants, with an exercise price of \$0.001 per warrant (the “2023 Pre-Funded Warrants” and together with the 2022 Warrants the “Warrants”), that we issued in a private placement completed on April 27, 2023.

Investing in our securities involves a number of risks. See “Risk Factors” on page 6 and other risk factors contained in the documents incorporated by referenced herein before you make your investment decision.

We or the selling stockholders may offer securities through underwriting syndicates managed or co-managed by one or more underwriters or dealers, through agents or directly to purchasers. If required, the prospectus supplement for each offering of securities will describe the plan of distribution for that offering. For general information about the distribution of securities offered, please see “Plan of Distribution” in this prospectus.

We do not know when or in what amount the selling stockholders may offer the shares for sale. We will not receive any proceeds from the sale of shares of common stock by the selling stockholders, except with respect to amounts received by us upon exercise of the Warrants, to the extent such Warrants are exercised for cash.

We have agreed to pay certain expenses related to the registration of the offer and sale of the shares of common stock pursuant to the registration statement of which this prospectus forms a part. The selling stockholders will bear all commissions and discounts, if any, attributable to the sale of the shares by the selling stockholders.

Our common stock is listed on The Nasdaq Global Market under the trading symbol “APLT.” On May 8, 2023, the last reported price of our common stock was \$1.51 per share. Each prospectus supplement will indicate whether the securities offered thereby will be listed on any securities exchange.

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

The date of this prospectus is May 19, 2023

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission (the “SEC”), using a “shelf” registration process.

Under this process, we may sell from time to time any combination of the securities described in this prospectus in one or more offerings up to a total price to the public of \$300,000,000. We may also use this prospectus to issue up to 38,250,000 shares of our common stock, par value \$0.0001 per share, upon the exercise of (i) 8,250,000 outstanding pre-funded warrants, with an exercise price of \$0.001 per warrant (the “2022 Pre-Funded Warrants”), and (ii) 30,000,000 outstanding common warrants, with an exercise price of \$1.00 per warrant (the “2022 Common Warrants” and together with the 2022 Pre-Funded Warrants the “2022 Warrants”), that we previously issued in a public offering pursuant to a registration statement on Form S-3 on June 22, 2022. In addition, the selling stockholders may offer and sell from time to time up to 31,735,731 shares of our common stock, of which 22,000,000 shares are issuable upon the exercise of pre-funded warrants, with an exercise price of \$0.001 per warrant (the “2023 Pre-Funded Warrants” and together with the 2022 Warrants the “Warrants”), that we issued in a private placement completed on April 27, 2023 (the “2023 Private Placement”). The offer and sale of securities under this prospectus may be made from time to time, in one or more offerings, in any manner described under the section in this prospectus entitled “Plan of Distribution.”

This prospectus only provides you with a general description of the securities that we may offer. Each time we sell securities, we will, and each time the selling stockholders sell securities, the selling stockholders may, if required, provide a supplement to this prospectus that contains specific information about the terms of that offering, including the specific amounts, prices and terms of the securities offered. 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, any accompanying prospectus supplement and any free writing prospectus prepared by or on behalf of us, together with the additional information described under the heading “Where You Can Find More Information.”

Neither we, nor the selling stockholders, has authorized anyone to provide you with any information other than that contained in or incorporated by reference into this prospectus, any accompanying prospectus supplement and any free writing prospectus prepared by or on behalf of us. We and the selling stockholders take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We and the selling stockholders are not making offers to sell the securities in any jurisdiction in which an offer or solicitation is not authorized or in which the person making such offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make an offer or solicitation.

The information in this prospectus is accurate as of the date on the front cover. You should not assume that the information contained in this prospectus is accurate as of any other date.

When used in this prospectus, the terms “Applied,” “Applied Therapeutics,” the “company,” “we,” “our” and “us” refer to Applied Therapeutics, Inc., unless otherwise specified or the context otherwise requires.

“Applied Therapeutics,” the Applied Therapeutics logo and other trademarks, trade names or service marks of Applied Therapeutics, Inc. appearing in this prospectus are the property of Applied Therapeutics, Inc. All other trademarks, trade names and service marks appearing in this prospectus are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus may be referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert their rights thereto.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC under the Securities Exchange Act of 1934, as amended (the “Exchange Act”). Our SEC filings are available to the public at the SEC’s website at www.sec.gov.

The SEC allows us to “incorporate by reference” information into this prospectus and any accompanying prospectus supplement, 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 any accompanying prospectus supplement, except for any information superseded by information contained directly in this prospectus, any accompanying prospectus supplement, any subsequently filed document deemed incorporated by reference or any free writing prospectus prepared by or on behalf of us. This prospectus and any accompanying prospectus supplement incorporate by reference the documents set forth below that we have previously filed with the SEC (other than information deemed furnished and not filed in accordance with SEC rules, including Items 2.02 and 7.01 of Form 8-K):

- [our Annual Report on Form 10-K for the fiscal year ended December 31, 2022, filed with the SEC on March 23, 2023;](#)
- the information specifically incorporated by reference into our [Annual Report on Form 10-K for the fiscal year ended December 31, 2022](#) from our [definitive proxy statement on Schedule 14A, filed with the SEC on April 17, 2023;](#)
- [our Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2023, filed with the SEC on May 11, 2023;](#)
- our Current Reports on Form 8-K, filed with the SEC on [January 4, 2023](#), [February, 24, 2023](#), [April 14, 2023](#), [April 24, 2023](#) (other than information furnished under Item 7.01), and [April 27, 2023](#); and
- the description of our common stock contained in our Registration Statement on [Form 8-A, filed with the SEC on May 6, 2019](#), and any amendment or report filed for the purpose of updating such description, including [Exhibit 4.9 to our Annual Report on Form 10-K for the year ended December 31, 2022, filed with the SEC on March 23, 2023.](#)

All documents filed by us pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (i) after the date of the initial filing of the registration statement of which this prospectus is a part and prior to effectiveness of the registration statement and (ii) after the date of this prospectus and before the termination of the offering also shall be deemed to be incorporated herein by reference. We are not, however, incorporating by reference any documents or portions thereof that are not deemed “filed” with the SEC, including any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K.

Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, including any amendments to those reports, and other information that we file with or furnish to the SEC pursuant to Section 13(a) or 15(d) of the Exchange Act, can also be accessed free of charge from our website at <http://www.appliedtherapeutics.com>. These filings will be available as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Information contained on our website is not part of this prospectus.

You may request a free copy of any of the documents incorporated by reference in this prospectus (other than exhibits, unless they are specifically incorporated by reference in the documents) by writing or telephoning us at the following address:

Applied Therapeutics, Inc.
545 Fifth Avenue, Suite 1400
New York, NY 10017
(212) 220-9226

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and any accompanying prospectus supplement and any documents incorporated by reference contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 (the “Securities Act”), and Section 21E of the Securities Exchange Act of 1934 (the “Exchange Act”) about us and our industry that involve substantial risks and uncertainties. All statements other than statements of historical fact contained in this prospectus and any accompanying prospectus supplement and any documents incorporated by reference, including statements regarding our strategy, future financial condition, future operations, projected costs, prospects, plans, objectives of management and expected market growth, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “aim,” “anticipate,” “assume,” “believe,” “contemplate,” “continue,” “could,” “design,” “due,” “estimate,” “expect,” “forecast,” “goal,” “intend,” “may,” “objective,” “opportunity,” “plan,” “predict,” “project,” “positioned,” “potential,” “seek,” “should,” “target,” “will,” “would” and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology.

We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. These forward-looking statements are subject to a number of known and unknown risks, uncertainties and assumptions, including risks described in the section titled “Risk Factors” and elsewhere in this prospectus and any accompanying prospectus supplement and any documents incorporated by reference, regarding, among other things:

- our plans to develop, market and commercialize our product candidates;
- the initiation, timing, progress and results of our current and future preclinical studies and clinical trials and our research and development programs;
- our ability to take advantage of expedited regulatory pathways for any of our product candidates;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our ability to successfully acquire or license additional product candidates on reasonable terms and advance product candidates into, and successfully complete, clinical studies;
- our ability to maintain and establish collaborations or obtain additional funding;
- our ability to obtain and timing of regulatory approval of our current and future product candidates;
- the anticipated indications for our product candidates, if approved;
- our expectations regarding the potential market size and the rate and degree of market acceptance of such product candidates;
- our ability to fund our working capital requirements and expectations regarding the sufficiency of our capital resources;
- the implementation of our business model and strategic plans for our business and product candidates;
- our intellectual property position and the duration of our patent rights;
- developments or disputes concerning our intellectual property or other proprietary rights;
- the potential impact of the Covid-19 pandemic on the timing and progress of our ongoing clinical trials, our business, results of operations, liquidity, and operations and our ability to mitigate those potential impacts;
- our expectations regarding government and third-party payor coverage and reimbursement;
- our ability to compete in the markets we serve;
- the impact of government laws and regulations and liabilities thereunder;
- developments relating to our competitors and our industry; and

- other factors that may impact our financial results.

The foregoing list of factors is not exhaustive. Moreover, we operate in a very competitive and rapidly changing environment. New risk factors emerge from time to time, and it is not possible for our management to predict all risk factors nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements.

In light of the significant uncertainties in these forward-looking statements, you should not rely upon forward-looking statements as predictions of future events. Although we believe that we have a reasonable basis for each forward-looking statement contained in this prospectus and any accompanying prospectus supplement and any documents incorporated by reference, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur at all. You should refer to the section titled “Risk Factors” in this prospectus, any accompanying prospectus supplement or documents incorporated by reference for discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. Except as required by law, we undertake no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.

THE COMPANY

Overview

We are a clinical-stage biopharmaceutical company developing a pipeline of novel product candidates against validated molecular targets in indications of high unmet medical need. We focus on molecules and pathways whose role in the disease process is well known based on prior research, but have previously failed to yield successful products due to poor efficacy and tolerability. Our unique approach to drug development leverages recent technological advances to design improved drugs, employs early use of biomarkers to confirm biological activity and focuses on abbreviated regulatory pathways. Our first molecular target is aldose reductase, or AR, an enzyme that converts glucose to sorbitol under oxidative stress conditions, and is implicated in multiple diseases. Prior attempts to inhibit this enzyme were hindered by nonselective, nonspecific inhibition, which resulted in limited efficacy and significant off-target safety effects. The detrimental consequences of AR activation have been well established by decades of prior research. Our AR program currently includes three small molecules, which are all potent and selective inhibitors of AR, but are engineered to have unique tissue permeability profiles to target different disease states, including diabetic complications, heart disease and rare metabolic diseases. The result of this unique multifaceted approach to drug development is a portfolio of highly specific and selective product candidates that we believe are significantly de-risked and can move quickly through the development process.

Our Corporate Information

We were incorporated under the laws of the State of Delaware on January 20, 2016. Our principal executive offices are located at 545 Fifth Avenue, Suite 1400, New York, New York 10017, and our telephone number is (212) 220-9226. Our corporate website address is www.appliedtherapeutics.com. Information contained on, or accessible through, our website is not a part of this prospectus. We have included our website in this prospectus solely as an inactive textual reference.

RISK FACTORS

Investing in our securities involves risk. See the risk factors described in our most recent Annual Report on Form 10-K or Quarterly Report on Form 10-Q, as applicable, and those contained in our other filings with the SEC that are incorporated by reference in this prospectus and any accompanying prospectus supplement. Before making an investment decision, you should carefully consider these risks as well as other information we include or incorporate by reference in this prospectus and any accompanying prospectus supplement. These risks could materially affect our business, financial condition or results of operations and cause the value of our securities to decline. You could lose all or part of your investment.

USE OF PROCEEDS

All shares of common stock offered by the selling stockholders pursuant to this prospectus will be sold by the selling stockholders for their respective accounts. We will not receive any of the proceeds from these sales.

We will receive up to an aggregate of approximately \$30.2 million from the exercise of all of the Warrants, assuming the exercise in full of all of the Warrants for cash.

Except as otherwise set forth in any accompanying prospectus supplement, we expect to use the net proceeds from the sale of securities offered by us, as well as from the exercise of the Warrants, if any, for general corporate purposes. General corporate purposes may include research and development costs, including the conduct of clinical trials and process development and manufacturing of our product candidates, expansion of our research and development capabilities, working capital and capital expenditures.

SELLING STOCKHOLDERS

This prospectus relates to the possible resale by the selling stockholders of up to 31,735,731 shares of common stock of which, 22,000,000 shares are issuable upon the exercise the 2023 Pre-Funded Warrants. The term “selling stockholder” includes the stockholders listed below and their transferees, pledges, donees or other successors in interest selling shares received after the date of this prospectus from a selling stockholder as a gift, pledge, partnership distribution or other non-sale related transfer. Information concerning the selling stockholders may change after the date of this prospectus and changed information will be presented in a supplement to this prospectus if and when required.

The table below sets forth certain information with respect to each selling stockholder, including (i) the name of each selling stockholder; (ii) the number of shares of our common stock beneficially owned by each selling stockholder immediately following the 2023 Private Placement, without taking account of limitations on exercise of the selling stockholders’ Warrants; (iii) the maximum number of shares being offered by each selling stockholder pursuant to this prospectus without taking account of limitations on exercise of the selling stockholders’ Warrants; and (iv) each selling stockholder’s beneficial ownership after completion of this offering, assuming that all of the shares covered hereby (but no other shares, if any, held by the selling stockholders) are sold.

Holder of Warrants may not exercise any Warrants that would cause the aggregate number of shares of common stock beneficially owned by the holder to exceed 9.99% of the Company’s outstanding common stock immediately after exercise. Holders of the 2022 Warrants (together with affiliates) who immediately prior to the issue date beneficially owned more than 9.99% of outstanding common stock may not exercise any portion of their 2022 Warrants if the holder (together with affiliates) would beneficially own more than 19.99% of the Company’s outstanding common stock after exercise.

The table is based on information supplied to us by the selling stockholders, with beneficial ownership and percentage ownership determined in accordance with the rules and regulations of the SEC, and includes information with respect to voting or investment power with respect to shares of stock. This information does not necessarily indicate beneficial ownership for any other purpose.

The percentage of each selling stockholder’s ownership before and after this offering is based on 57,849,292 shares of common stock outstanding as of May 10, 2023, which includes the 9,735,731 shares of our common stock registered for resale by the selling stockholders in this offering.

The registration of the sale of shares of common stock held by and issuable to the selling stockholders does not mean that the selling stockholders will sell or otherwise dispose of all or any of those securities. The selling stockholders may sell or otherwise dispose of all, a portion or none of such shares from time to time.

The number of common stock in the column “Shares Offered Hereby” represents all of the common stock that such selling stockholder may offer and sell from time to time under this prospectus. This table is based upon information supplied to us by the selling stockholders and information filed with the SEC. The selling stockholders may sell or transfer all or a portion of their ordinary shares pursuant to any available exemption from registration requirements of the Securities Act. We do not know the number of shares, if any, that will be offered for sale or other disposition by any of the selling stockholders under this prospectus. Furthermore, the selling stockholders may have sold, transferred or disposed of the shares of common stock covered hereby in transactions exempt from the registration requirements of the Securities Act since the date on which we filed this prospectus.

Selling Stockholder	Beneficial Ownership Before this Offering		Shares Offered Hereby	Beneficial Ownership After this Offering	
	Number of Shares Owned	Percentage of Outstanding Shares		Number of Shares Owned ⁽¹⁾	Percentage of Outstanding Shares
Venrock Healthcare Capital Partners III, L.P. ⁽²⁾⁽³⁾	5,562,447	8.98%	5,562,447	—	—
VHCP Co-Investment Holdings III, LLC ⁽²⁾⁽⁴⁾	556,456	*	556,456	—	—
Venrock Healthcare Capital Partners EG, L.P. ⁽²⁾⁽⁵⁾	15,039,131	21.84%	15,039,131	—	—
PB SPV-I LLC ⁽⁶⁾	3,703,223	6.06%	3,703,223	—	—
Propel Bio Partners LP ⁽⁷⁾	3,432,824	5.84%	1,058,063	2,374,761	4.11%
Richard & Suzanne Kayne Living Trust dtd 01/14/1999 ⁽⁸⁾	2,645,163	4.40%	2,645,163	—	—
Franklin Strategic Series – Franklin Biotechnology Discovery Fund ⁽⁹⁾	5,026,154	8.34%	1,008,400	4,017,754	6.66%
Franklin Templeton Investment Funds – Franklin Biotechnology Discovery Fund ⁽¹⁰⁾	10,420,578	16.57%	2,162,848	8,257,730	13.13%
Total⁽¹¹⁾:	46,385,976	53.10%	31,735,731	14,650,245	22.42%

* Represents beneficial ownership of less than one percent (1%) of the outstanding shares of our common stock.

- (1) Assumes sale of all of the shares of common stock offered hereby.
- (2) VHCP Management III, LLC (“VHCPM III”) is the sole general partner of Venrock Healthcare Capital Partners III, L.P. (“VHCP III”) and the sole manager of VHCP Co-Investment Holdings III, LLC (“VHCP Co-III”). VHCP Management EG, LLC (“VHCPM EG”) is the sole general partner of Venrock Healthcare Capital Partners EG, L.P. (“VHCP EG”). Dr. Bong Koh and Nimish Shah are the voting members of VHCPM III and VHCPM EG. The address of the entities and individual listed above is 7 Bryant Park, 23rd Floor, New York, NY 10018.
- (3) Consists of (i) 1,487,497 shares and (ii) 4,074,950 shares issuable upon the exercise of 2023 Pre-Funded Warrants.
- (4) Consists of (i) 148,806 shares and (ii) 407,650 shares issuable upon the exercise of 2023 Pre-Funded Warrants.
- (5) Consists of (i) 4,021,731 shares and (ii) 11,017,400 shares issuable upon the exercise of 2023 Pre-Funded Warrants.
- (6) Consists of (i) 453,224 shares and (ii) 3,249,999 shares issuable upon the exercise of 2023 Pre-Funded Warrants. Leen Kawas is the managing member of PB SPV-I LLC. Ms. Kawas disclaims beneficial ownership over all shares held by PB SPV-I LLC except to the extent of her respective indirect pecuniary interests therein. The address of the entities and individual listed above is 1800 Avenue of the Stars, 3rd Floor, Los Angeles, CA 90067.
- (7) Consists of (i) 2,504,253 shares and (ii) 928,571 shares issuable upon the exercise of 2023 Pre-Funded Warrants. 1800 Avenue of the Stars, 3rd Floor, Los Angeles, CA 90067. Leen Kawas is the managing member of Propel Bio Partners LP. Ms. Kawas disclaims beneficial ownership over all shares held by Propel Bio Partners LP except to the extent of her indirect pecuniary interests therein. The address of the entities and individual listed above is 1800 Avenue of the Stars, 3rd Floor, Los Angeles, CA 90067.
- (8) Consists of (i) 323,733 shares and (ii) 2,321,430 shares issuable upon the exercise of 2023 Pre-Funded Warrants. Richard & Suzanne Kayne Living Trust dtd 01/14/1999, of which Richard Kayne is Trustee, has a business address of 1900 Avenue of the Stars, #1000, Los Angeles, CA 90067. Representatives of the selling stockholder have advised us that the selling stockholder is an affiliate of a U.S. registered

broker-dealer; however, the selling stockholder acquired the securities in the ordinary course of business and, at the time of the acquisition, had no agreements or understandings, directly or indirectly, with any party to distribute the securities held by the selling stockholder.

- (9) Consists of (i) 2,584,054 shares and (ii) 2,442,100 shares issuable upon the exercise of 814,000 2022 Pre-Funded Warrants and 1,628,100 2022 Common Warrants. Franklin Advisers, Inc. (“FAV”) is the investment manager for Franklin Strategic Series — Franklin Biotechnology Discovery Fund. Evan McCulloch has power to vote and/or power to dispose of the securities held by Franklin Strategic Series — Franklin Biotechnology Discovery Fund as the Senior Vice President of FAV, the investment manager of Franklin Strategic Series — Franklin Biotechnology Discovery Fund and disclaims beneficial ownership of the shares held by Franklin Strategic Series — Franklin Biotechnology Discovery Fund. The address of the fund is One Franklin Parkway, San Mateo, CA 99403.
- (10) Consists of (i) 5,362,678 shares and (ii) 5,057,900 shares issuable upon the exercise of 1,686,000 2022 Pre-Funded Warrants and 3,371,900 2022 Common Warrants. Franklin Advisers, Inc. (“FAV”) is the investment manager for Franklin Templeton Investment Funds — Franklin Biotechnology Discovery Fund. Evan McCulloch has power to vote and/or power to dispose of the securities held by Franklin Templeton Investment Funds — Franklin Biotechnology Discovery Fund as the Senior Vice President of FAV, the investment manager of Franklin Templeton Investment Funds — Franklin Biotechnology Discovery Fund and disclaims beneficial ownership of the shares held by the Franklin Templeton Investment Funds — Franklin Biotechnology Discovery Fund. The address of the fund is One Franklin Parkway, San Mateo, CA 99403.
- (11) The number of shares beneficially owned after this offering consists of (i) 7,150,245 shares and (ii) 7,500,000 shares issuable upon the exercise of 2,500,000 2022 Pre-Funded Warrants and 5,000,000 2022 Common Warrants.

DESCRIPTION OF SECURITIES

This prospectus contains summary descriptions of the common stock, preferred stock, depository shares, debt securities and warrants that may be offered and sold from time to time. These summary descriptions are not meant to be complete descriptions of each security. However, at the time of an offering and sale, this prospectus together with the accompanying prospectus supplement will contain the material terms of the securities being offered.

DESCRIPTION OF CAPITAL STOCK

General

The following summary description of our capital stock is based on the provisions of the General Corporation Law of the State of Delaware (the “DGCL”), our amended and restated certificate of incorporation and our amended and restated bylaws. This description does not purport to be complete and is qualified in its entirety by reference to the full text of the DGCL, as it may be amended from time to time, and to the terms of our amended and restated certificate of incorporation and amended and restated bylaws, as each may be amended from time to time, which are incorporated by reference as exhibits to the registration statement of which this prospectus is a part. See “Where You Can Find More Information.” As used in this “Description of Capital Stock,” the terms “Applied,” “Applied Therapeutics,” the “company,” “we,” “our” and “us” refer to Applied Therapeutics, Inc., a Delaware corporation.

Our authorized capital stock consists of 200,000,000 shares of common stock, par value \$0.0001 per share, and 10,000,000 shares of preferred stock, par value \$0.0001 per share. The number of authorized shares of any class may be increased or decreased by an amendment to our amended and restated certificate of incorporation proposed by our board of directors and approved by an affirmative vote of the holders of shares of capital stock of the company representing a majority of the votes represented by all outstanding shares of capital stock of the company entitled to vote. As of May 11, 2023, 57,849,292 shares of common stock were issued and outstanding and no shares of preferred stock were issued and outstanding.

Common Stock

Voting Rights

Each holder of common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders. Our common stockholders will not be entitled to cumulate their votes in the election of directors. Generally, all matters to be voted on by stockholders must be approved by a majority (or, in the case of election of directors, by a plurality) of the votes entitled to be cast by all holders of our common stock present in person or represented by proxy, voting together as a single class. Except as otherwise provided by law, amendments to our amended and restated certificate of incorporation must be approved by the affirmative vote of holders of at least a majority (and, in some cases, sixty-six and two-thirds percent (66 $\frac{2}{3}$ %) of the voting power of all of the then-outstanding shares of capital stock entitled to vote generally in the election of directors, voting in a single class. Except as otherwise provided by law, amendments to our amended and restated bylaws must be approved by an affirmative vote of the holders of at least sixty-six and two-thirds percent (66 $\frac{2}{3}$ %) of the voting power of all the then-outstanding shares of the capital stock of the company entitled to vote generally in the election of directors, voting together as a single class.

Dividends

Subject to preferences that may apply to any outstanding preferred stock, holders of our common stock are entitled to receive ratably any dividends that our board of directors may declare out of funds legally available for that purpose on a non-cumulative basis.

Liquidation

In the event of our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of

our debts and other liabilities, subject to the satisfaction of any liquidation preference granted to the holders of any outstanding shares of preferred stock.

Rights and Preferences

Holders of our common stock have no preemptive, conversion or subscription rights, and there are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences and privileges of the holders of our common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of our preferred stock that we may designate and issue in the future.

Registration Rights

Purchasers of our common stock and 2023 Pre-Funded Warrants in the 2023 Private Placement are entitled to certain rights with respect to registration of such shares of common stock and shares issuable upon exercise of the 2023 Pre-Funded Warrants under the Securities Act. These shares are referred to herein as “registrable securities.” The holders of these registrable securities possess registration rights pursuant to the terms of the registration rights agreement, by and among us and certain of our stockholders, dated as of April 23, 2023 (the “Registration Rights Agreement”). The registration of shares of our common stock and shares issuable upon exercise of 2023 Pre-Funded Warrants pursuant to the exercise of such registration rights would enable the holders to trade these shares without restriction under the Securities Act when the applicable registration statement is declared effective. We will pay the registration expenses, other than underwriting discounts, selling commissions and stock transfer taxes, of the shares registered pursuant to the registration of such securities on Form S-3 as described in the Registration Rights Agreement.

The Company shall have no further obligations pursuant to the Registration Rights Agreement at the earlier of (i) such time as no registrable securities are outstanding and (ii) such time as the registrable securities covered by the this registration statement that are not held by Affiliates of the Company are, as determined by the Company, eligible for resale pursuant to Rule 144 without limitation, restriction or condition (including any current public information requirement thereunder).

Preferred Stock

This section describes the general terms and provisions of preferred stock that we are authorized to issue. An accompanying prospectus supplement will describe the specific terms of the shares of preferred stock offered through that prospectus supplement, as well as any general terms described in this section that will not apply to those shares of preferred stock. If there are differences between the prospectus supplement relating to a particular series of preferred stock and this prospectus, the prospectus supplement will control. We will file a copy of the certificate of amendment to our amended and restated certificate of incorporation that contains the terms of each new series of preferred stock with the Secretary of the State of Delaware and with the SEC each time we issue a new series of preferred stock. Each such certificate of amendment will establish the number of shares included in a designated series and fix the designation, powers, privileges, preferences and rights of the shares of each series as well as any applicable qualifications, limitations or restrictions. As of the date of this prospectus, there are no restrictions on the repurchase or redemption of our preferred shares while there is any arrearage in the payment of dividends or sinking fund installments. You should refer to the applicable certificate of amendment as well as our amended and restated certificate of incorporation before deciding to buy shares of our preferred stock as described in any accompanying prospectus supplement.

Our board of directors has been authorized to provide for the issuance of up to 10,000,000 shares of our preferred stock in multiple series without the approval of shareholders. With respect to each series of our preferred stock, our board of directors has the authority to fix the following terms:

- the designation of the series, which may be by distinguishing number, letter or title;
- the number of shares within the series;
- whether dividends are cumulative and, if cumulative, the dates from which dividends are cumulative;
- the rate of any dividends, any conditions upon which dividends are payable, and the dates of payment of dividends;

- whether the shares are redeemable, the redemption price and the terms of redemption;
- the amount payable for each share if we dissolve or liquidate;
- whether the shares are convertible or exchangeable, the price or rate of conversion or exchange, and the applicable terms and conditions;
- any restrictions on issuance of shares in the same series or any other series;
- voting rights applicable to the series of preferred stock; and

any other rights, priorities, preferences, restrictions or limitations of such series.

The right of a holder of preferred stock to receive payment in respect thereof upon any liquidation, dissolution or winding up of us will be subordinate to the rights of our general creditors.

Anti-Takeover Provisions of Delaware Law and Our Charter Documents

Section 203 of the Delaware General Corporation Law

We are subject to Section 203 of the DGCL, which prohibits a Delaware corporation from engaging in any business combination with any interested stockholder for a period of three years after the date that such stockholder became an interested stockholder, with the following exceptions:

- before such date, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;
- upon completion of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction began, excluding for purposes of
- determining the voting stock outstanding (but not the outstanding voting stock owned by the interested stockholder) those shares owned (i) by persons who are directors and also officers and (ii) employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- on or after such date, the business combination is approved by the board of directors and authorized at an annual or special meeting of the stockholders, and not by written consent, by the affirmative vote of at least 66 $\frac{2}{3}$ % of the outstanding voting stock that is not owned by the interested stockholder.

In general, Section 203 defines a “business combination” to include the following:

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

In general, Section 203 defines an “interested stockholder” as an entity or person who, together with the person’s affiliates and associates, beneficially owns, or within three years prior to the time of determination of interested stockholder status did own, 15% or more of the outstanding voting stock of the corporation.

The statute could prohibit or delay mergers or other takeover or change in control attempts and, accordingly, may discourage attempts to acquire us even though such a transaction may offer our stockholders the opportunity to sell their stock at a price above the prevailing market price.

Amended and Restated Certificate of Incorporation, Amended and Restated Bylaws and Other Agreements

Among other things, our amended and restated certificate of incorporation and amended and restated bylaws:

- permit our board of directors to issue up to 10,000,000 shares of preferred stock, with any rights, preferences and privileges as they may designate, including the right to approve an acquisition or other change in control;
- provide that the authorized number of directors may be changed only by resolution of our board of directors;
- provide that our board of directors be classified into three classes of directors;
- provide that, subject to the rights of any series of preferred stock to elect directors, directors may only be removed for cause, which removal may be effected, subject to any limitation imposed by law, by the holders of at least sixty-six and two-thirds percent (66 $\frac{2}{3}$ %) of the voting power of all of our then-outstanding shares of the capital stock entitled to vote generally at an election of directors;
- provide that all vacancies, including newly created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum;
- 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 or electronic transmission;
- 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 advance notice in writing, and also specify requirements as to the form and content of a stockholder's notice;
- provide that special meetings of our stockholders may be called only by the chairman of our board of directors, our chief executive officer or by our board of directors pursuant to a resolution adopted by a majority of the total number of authorized directors; and
- 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.

The amendment of any of these provisions would require, in the case of provisions of the amended and restated certificate of incorporation, approval by affirmative vote of holders of at least a majority of the voting power of all of the then-outstanding shares of capital stock, voting as a single class, and in the case of provisions of the amended and restated bylaws, approval by affirmative vote of the holders of at least sixty-six and two-thirds percent (66 $\frac{2}{3}$ %) of the voting power of all the then-outstanding shares of the capital stock of the company entitled to vote generally in the election of directors, voting together as a single class.

The combination of these provisions make it more difficult for our existing stockholders to replace our board of directors as well as for another party to obtain control of us by replacing our board of directors. Because our board of directors has the power to retain and discharge our officers, these provisions could also make it more difficult for existing stockholders or another party to effect a change in management. In addition, the authorization of undesignated preferred stock makes it possible for our board of directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to change our control.

These provisions are intended to enhance the likelihood of continued stability in the composition of our board of directors and its policies and to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to reduce our vulnerability to hostile takeovers and to discourage certain tactics that may be used in proxy fights. However, such provisions could have the effect of discouraging others from making tender offers for our shares and may have the effect of delaying changes in our control or management. As a consequence, these provisions may also inhibit fluctuations in the market price of our stock that could result from actual or rumored takeover attempts. We believe that the benefits of these provisions, including increased protection of our potential ability to negotiate with the proponent of an

unfriendly or unsolicited proposal to acquire or restructure our company, outweigh the disadvantages of discouraging takeover proposals, because negotiation of takeover proposals could result in an improvement of their terms.

Choice of Forum

Our amended and restated certificate of incorporation provides that, with respect to any state actions or proceedings under Delaware statutory or common law, the Court of Chancery of the State of Delaware will be the exclusive forum for any derivative action or proceeding brought on our behalf; any action asserting a breach of fiduciary duty; any action asserting a claim against us arising pursuant to the DGCL, our amended and restated certificate of incorporation or our amended and restated bylaws; or any action asserting a claim against us that is governed by the internal affairs doctrine. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with one or more actions or proceedings described above, a court could find the choice of forum provisions contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable.

Our amended and restated bylaws provides that, unless we consent in writing to the selection of an alternative forum (an "Alternative Forum Consent"), the federal district courts of the United States of America will, 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. The existence of any prior Alternative Forum Consent will not act as a waiver of our ongoing consent right with respect to any current or future actions or claims arising under the Securities Act.

Listing

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

Transfer Agent and Registrar

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

DESCRIPTION OF DEPOSITARY SHARES

We may offer depositary receipts representing fractional shares of our preferred stock, rather than full shares of preferred stock. The shares of preferred stock represented by depositary shares will be deposited under a depositary agreement between us and a bank or trust company that meets certain requirements and is selected by us (the “Bank Depositary”). Each owner of a depositary share will be entitled to all the rights and preferences of the preferred stock represented by the depositary share.

The description in an accompanying prospectus supplement of any depositary shares we offer will not necessarily be complete and will be qualified in its entirety by reference to the applicable depositary agreement, which will be filed with the SEC if we offer depositary shares. For more information on how you can obtain copies of any depositary agreement if we offer depositary shares, see “Where You Can Find More Information.” We urge you to read the applicable depositary agreement and any accompanying prospectus supplement in their entirety.

Dividends and Other Distributions

If we pay a cash distribution or dividend on a series of preferred stock represented by depositary shares, the Bank Depositary will distribute such dividends to the record holders of such depositary shares. If the distributions are in property other than cash, the Bank Depositary will distribute the property to the record holders of the depositary shares. However, if the Bank Depositary determines that it is not feasible to make the distribution of property, the Bank Depositary may, with our approval, sell such property and distribute the net proceeds from such sale to the record holders of the depositary shares.

Redemption of Depositary Shares

If we redeem a series of preferred stock represented by depositary shares, the Bank Depositary will redeem the depositary shares from the proceeds received by the Bank Depositary in connection with the redemption. The redemption price per depositary share will equal the applicable fraction of the redemption price per share of the preferred stock. If fewer than all the depositary shares are redeemed, the depositary shares to be redeemed will be selected by lot or pro rata as the Bank Depositary may determine.

Voting the Preferred Stock

Upon receipt of notice of any meeting at which the holders of the preferred stock represented by depositary shares are entitled to vote, the Bank Depositary will mail the notice to the record holders of the depositary shares relating to such preferred stock. Each record holder of these depositary shares on the record date, which will be the same date as the record date for the preferred stock, may instruct the Bank Depositary as to how to vote the preferred stock represented by such holder’s depositary shares. The Bank Depositary will endeavor, insofar as practicable, to vote the amount of the preferred stock represented by such depositary shares in accordance with such instructions, and we will take all action that the Bank Depositary deems necessary in order to enable the Bank Depositary to do so. The Bank Depositary will abstain from voting shares of the preferred stock to the extent it does not receive specific instructions from the holders of depositary shares representing such preferred stock.

Amendment and Termination of the Depositary Agreement

The form of depositary receipt evidencing the depositary shares and any provision of the depositary agreement may be amended by agreement between the Bank Depositary and us. However, any amendment that materially and adversely alters the rights of the holders of depositary shares will not be effective unless such amendment has been approved by the holders of at least a majority of the depositary shares then outstanding. The depositary agreement may be terminated by the Bank Depositary or us only if (1) all outstanding depositary shares have been redeemed or (2) there has been a final distribution in respect of the preferred stock in connection with any liquidation, dissolution or winding up of our company and such distribution has been distributed to the holders of depositary receipts.

DESCRIPTION OF DEBT SECURITIES

We may offer debt securities in one or more series, which may be senior debt securities or subordinated debt securities and which may be convertible into another security.

The following description briefly sets forth certain general terms and provisions of the debt securities. The particular terms of the debt securities offered by any prospectus supplement and the extent, if any, to which the following general terms and provisions may apply to the debt securities, will be described in an accompanying prospectus supplement. Our debt securities will be issued in one or more series under an indenture to be entered into between us and a trustee to be named in a prospectus supplement, as amended or supplemented from time to time. A form of the indenture is attached as an exhibit to the registration statement of which this prospectus forms a part. The terms of the debt securities will include those set forth in the indenture and those made a part of the indenture by the Trust Indenture Act of 1939 (“TIA”). You should read the summary below, any accompanying prospectus supplement and the provisions of the indenture in their entirety before investing in our debt securities.

The aggregate principal amount of debt securities that may be issued under the indenture is unlimited. The prospectus supplement relating to any series of debt securities that we may offer will contain the specific terms of the debt securities. These terms may include, among others, the following:

- the title and aggregate principal amount of the debt securities and any limit on the aggregate principal amount of such series;
- any applicable subordination provisions for any subordinated debt securities;
- the maturity date(s) or method for determining same;
- the interest rate(s) or the method for determining same;
- the dates on which interest will accrue or the method for determining dates on which interest will accrue and dates on which interest will be payable and whether interest will be payable in cash, additional securities or some combination thereof;
- whether the debt securities are convertible or exchangeable into other securities and any related terms and conditions;
- redemption or early repayment provisions;
- authorized denominations;
- if other than the principal amount, the principal amount of debt securities payable upon acceleration;
- place(s) where payment of principal and interest may be made, where debt securities may be presented and where notices or demands upon the company may be made;
- the form or forms of the debt securities of the series including such legends as may be required by applicable law;
- whether the debt securities will be issued in whole or in part in the form of one or more global securities and the date as of which the securities are dated if other than the date of original issuance;
- whether the debt securities are secured and the terms of such security;
- the amount of discount or premium, if any, with which the debt securities will be issued;
- any covenants applicable to the particular debt securities being issued;
- any additions or changes in the defaults and events of default applicable to the particular debt securities being issued;
- the guarantors of each series, if any, and the extent of the guarantees (including provisions relating to seniority, subordination and release of the guarantees), if any;
- the currency, currencies or currency units in which the purchase price for, the principal of and any premium and any interest on, the debt securities will be payable;

- the time period within which, the manner in which and the terms and conditions upon which we or the holders of the debt securities can select the payment currency;
- our obligation or right to redeem, purchase or repay debt securities under a sinking fund, amortization or analogous provision;
- any restriction or conditions on the transferability of the debt securities;
- provisions granting special rights to holders of the debt securities upon occurrence of specified events;
- additions or changes relating to compensation or reimbursement of the trustee of the series of debt securities;
- provisions relating to the modification of the indenture both with and without the consent of holders of debt securities issued under the indenture and the execution of supplemental indentures for such series; and
- any other terms of the debt securities (which terms shall not be inconsistent with the provisions of the TIA, but may modify, amend, supplement or delete any of the terms of the indenture with respect to such series of debt securities).

General

We may sell the debt securities, including original issue discount securities, at par or at a substantial discount below their stated principal amount. Unless we inform you otherwise in a prospectus supplement, we may issue additional debt securities of a particular series without the consent of the holders of the debt securities of such series or any other series outstanding at the time of issuance. Any such additional debt securities, together with all other outstanding debt securities of that series, will constitute a single series of securities under the indenture.

We will describe in an accompanying prospectus supplement any other special considerations for any debt securities we sell that are denominated in a currency or currency unit other than U.S. dollars. In addition, debt securities may be issued where the amount of principal and/or interest payable is determined by reference to one or more currency exchange rates, commodity prices, equity indices or other factors. Holders of such securities may receive a principal amount or a payment of interest that is greater than or less than the amount of principal or interest otherwise payable on such dates, depending upon the value of the applicable currencies, commodities, equity indices or other factors. Information as to the methods for determining the amount of principal or interest, if any, payable on any date, and the currencies, commodities, equity indices or other factors to which the amount payable on such date is linked will be described in an accompanying prospectus supplement.

United States federal income tax consequences and special considerations, if any, applicable to any such series will be described in an accompanying prospectus supplement.

We expect most debt securities to be issued in fully registered form without coupons and in denominations of \$2,000 and any integral multiple of \$1,000 in excess thereof. Subject to the limitations provided in the indenture and in an accompanying prospectus supplement, debt securities that are issued in registered form may be transferred or exchanged at the designated corporate trust office of the trustee, without the payment of any service charge, other than any tax or other governmental charge payable in connection therewith.

Global Securities

Unless we inform you otherwise in an accompanying prospectus supplement, the debt securities of a series may be issued in whole or in part in the form of one or more global securities that will be deposited with, or on behalf of, a depositary identified in an accompanying prospectus supplement. Unless and until a global security is exchanged in whole or in part for the individual debt securities, a global security may not be transferred except as a whole by the depositary for such global security to a nominee of such depositary or by a nominee of such depositary to such depositary or another nominee of such depositary or by such depositary or any such nominee to a successor of such depositary or a nominee of such successor.

Governing Law

The indenture and the debt securities shall be construed in accordance with and governed by the laws of the State of New York.

DESCRIPTION OF WARRANTS

We may issue warrants for the purchase of shares of our common stock, shares of preferred stock or our debt securities. We may issue warrants independently or together with other securities, and they may be attached to or separate from the other securities. Each series of warrants will be issued under a separate warrant agreement that we will enter into with a bank or trust company, as warrant agent, as detailed in an accompanying prospectus supplement. The warrant agent will act solely as our agent in connection with the warrants and will not assume any obligation, or agency or trust relationship, with you.

The prospectus supplement relating to a particular issue of warrants will describe the terms of those warrants, including, when applicable:

- the offering price;
- the currency or currencies, including composite currencies, in which the purchase price and/or exercise price of the warrants may be payable;
- the number of warrants offered;
- the exercise price and the amount of securities you will receive upon exercise;
- the procedure for exercise of the warrants and the circumstances, if any, that will cause the warrants to be automatically exercised;
- the rights, if any, we have to redeem the warrants;
- the date on which the right to exercise the warrants will commence and the date on which the warrants will expire;
- the name of the warrant agent; and
- any other material terms of the warrants.

After warrants expire they will become void. The prospectus supplement may provide for the adjustment of the exercise price of the warrants.

Warrants may be exercised at the appropriate office of the warrant agent or any other office indicated in an accompanying prospectus supplement. Before the exercise of warrants, holders will not have any of the rights of holders of the securities purchasable upon exercise and will not be entitled to payments made to holders of those securities.

The description in an accompanying prospectus supplement of any warrants we offer will not necessarily be complete and will be qualified in its entirety by reference to the applicable warrant agreement, which will be filed with the SEC if we offer warrants. For more information on how you can obtain copies of any warrant agreement if we offer warrants, see “Where You Can Find More Information.” We urge you to read the applicable warrant agreement and any accompanying prospectus supplement in their entirety.

PLAN OF DISTRIBUTION

Our Plan of Distribution

We may sell the securities offered by this prospectus from time to time in one or more transactions, including without limitation:

- through underwriters or dealers;
- directly to purchasers;
- in a rights offering;
- in “at the market” offerings, within the meaning of Rule 415(a)(4) of the Securities Act, to or through a market maker or into an existing trading market on an exchange or otherwise;
- through agents;
- through a combination of any of these methods; or
- through any other method permitted by applicable law and described in a prospectus supplement.

In addition, we may enter into derivative or hedging transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. In connection with such a transaction, the third parties may sell securities covered by and pursuant to this prospectus and any accompanying prospectus supplement. If so, the third party may use securities borrowed from us or others to settle such sales and may use securities received from us to close out any related short positions. We may also loan or pledge securities covered by this prospectus and any accompanying prospectus supplement to third parties, who may sell the loaned securities or, in an event of default in the case of a pledge, sell the pledged securities pursuant to this prospectus and any accompanying prospectus supplement.

The prospectus supplement with respect to any offering of securities will include the following information:

- the terms of the offering;
- the names of any underwriters, dealers or direct purchasers;
- the name or names of any managing underwriter or underwriters;
- the purchase price or initial public offering price of the securities;
- the net proceeds from the sale of the securities;
- any delayed delivery arrangements;
- any underwriting discounts, commissions and other items constituting underwriters’ compensation;
- any discounts or concessions allowed or reallocated or paid to dealers;
- any commissions paid to agents; and
- any securities exchange on which the securities may be listed.

Sale through Underwriters or Dealers

If underwriters are used in the sale, the underwriters will acquire the securities for their own account. The underwriters may resell the securities from time to time in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. Underwriters may offer securities to the public either through underwriting syndicates represented by one or more managing underwriters or directly by one or more firms acting as underwriters. Unless we inform you otherwise in the applicable prospectus supplement, the obligations of the underwriters to purchase the securities will be subject to certain conditions, and the underwriters will be obligated to purchase all of the offered securities if they purchase any of them. The underwriters may change from time to time any initial public offering price and any discounts or concessions allowed or reallocated or paid to dealers.

During and after an offering through underwriters, the underwriters may purchase and sell the securities in the open market. These transactions may include over-allotment and stabilizing transactions and purchases to cover syndicate short positions created in connection with the offering. The underwriters may also impose a penalty bid, which means that selling concessions allowed to syndicate members or other broker-dealers for the offered securities sold for their account may be reclaimed by the syndicate if the offered securities are repurchased by the syndicate in stabilizing or covering transactions. These activities may stabilize, maintain or otherwise affect the market price of the offered securities, which may be higher than the price that might otherwise prevail in the open market. If commenced, the underwriters may discontinue these activities at any time.

Some or all of the securities that we offer through this prospectus may be new issues of securities with no established trading market. Any underwriters to whom we sell our securities for public offering and sale may make a market in those securities, but they will not be obligated to do so and they may discontinue any market making at any time without notice. Accordingly, we cannot assure you of the liquidity of, or continued trading markets for, any securities that we offer.

If dealers are used in the sale of securities, we will sell the securities to them as principals. They may then resell those securities to the public at fixed prices or at varying prices determined by the dealers at the time of resale. We will include in the applicable prospectus supplement the names of the dealers and the terms of the transaction.

If agents are used in an offering, the names of the agents and the terms of the agency will be specified in a prospectus supplement. Unless otherwise indicated in a prospectus supplement, the agents will act on a best-efforts basis for the period of their appointment.

Dealers and agents named in a prospectus supplement may be underwriters as defined in the Securities Act and any discounts or commissions they receive from us and any profit on their resale of the securities may be treated as underwriting discounts and commissions under the Securities Act. We will identify in the applicable prospectus supplement any underwriters, dealers or agents and will describe their compensation. We may have agreements with the underwriters, dealers and agents to indemnify them against specified civil liabilities, including liabilities under the Securities Act.

Underwriters, dealers or agents and their associates may engage in other transactions with and perform other services for us in the ordinary course of business.

If so indicated in a prospectus supplement, we will authorize underwriters or other persons acting as our agents to solicit offers by institutional investors to purchase securities pursuant to contracts providing for payment and delivery on a future date. We may enter contracts with commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutional investors. The obligations of any institutional investor will be subject to the condition that its purchase of the offered securities will not be illegal at the time of delivery. The underwriters and other agents will not be responsible for the validity or performance of contracts.

Direct Sales and Sales through Agents

We may sell the securities directly. In this case, no underwriters or agents would be involved. We may also sell the securities through agents designated by us from time to time. In the applicable prospectus supplement, we will name any agent involved in the offer or sale of the offered securities, and we will describe any commissions payable to the agent. Unless we inform you otherwise in the applicable prospectus supplement, any agent will agree to use its reasonable best efforts to solicit purchases for the period of its appointment.

We may sell the securities directly to institutional investors or others who may be deemed to be underwriters within the meaning of the Securities Act with respect to any sale of those securities. We will describe the terms of any sales of these securities in the applicable prospectus supplement.

At the Market Offerings

We may also sell the securities offered by any applicable prospectus supplement in “at the market offerings” within the meaning of Rule 415(a)(4) of the Securities Act, to or through a market maker or into an existing trading market, on an exchange or otherwise.

Remarketing Arrangements

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

Delayed Delivery Contracts

If we so indicate in the applicable prospectus supplement, we may authorize agents, underwriters or dealers to solicit offers from certain types of institutions to purchase securities from us at the public offering price under delayed delivery contracts. These contracts would provide for payment and delivery on a specified date in the future.

The contracts would be subject only to those conditions described in the applicable prospectus supplement. The applicable prospectus supplement will describe the commission payable for solicitation of those contracts.

General Information

We may have agreements with the underwriters, dealers, agents and remarketing firms to indemnify them against certain civil liabilities, including liabilities under the Securities Act, or to contribute with respect to payments that the underwriters, dealers, agents or remarketing firms may be required to make. Underwriters, dealers, agents and remarketing firms may be customers of, engage in transactions with or perform services for us in the ordinary course of their businesses.

Selling Stockholders' Plan of Distribution

We are registering the shares of common stock issued to the selling stockholders to permit the resale of these shares of common stock by the holders of the shares of common stock from time to time after the date of this prospectus. We will not receive any of the proceeds from the sale by the selling stockholders of the shares of common stock. We will bear all fees and expenses incident to our obligation to register the shares of common stock.

The selling stockholders may sell all or a portion of the shares of common stock beneficially owned by them and offered hereby from time to time directly or through one or more underwriters, broker-dealers or agents. If the shares of common stock are sold through underwriters or broker-dealers, the selling stockholders will be responsible for underwriting discounts or commissions or agent's commissions. The shares of common stock may be sold on any national securities exchange or quotation service on which the securities may be listed or quoted at the time of sale, in the over-the-counter market or in transactions otherwise than on these exchanges or systems or in the over-the-counter market and in one or more transactions at fixed prices, at prevailing market prices at the time of the sale, at varying prices determined at the time of sale, or at negotiated prices. These sales may be effected in transactions, which may involve crosses or block transactions. The selling stockholders may use any one or more of the following methods when selling shares:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent, but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- settlement of short sales entered into after the effective date of the registration statement of which this prospectus is a part;
- broker-dealers may agree with the selling stockholders to sell a specified number of such shares at a stipulated price per share;

- through the writing or settlement of options or other hedging transactions, whether such options are listed on an options exchange or otherwise;
- a combination of any such methods of sale; and
- any other method permitted pursuant to applicable law.

The selling stockholders also may resell all or a portion of the shares in open market transactions in reliance upon Rule 144 under the Securities Act, as permitted by that rule, or Section 4(1) under the Securities Act, if available, rather than under this prospectus; *provided* that they meet the criteria and conform to the requirements of those provisions.

Broker dealers engaged by the selling stockholders may arrange for other broker dealers to participate in sales. If the selling stockholders effect such transactions by selling shares of common stock to or through underwriters, broker-dealers or agents, such underwriters, broker-dealers or agents may receive commissions in the form of discounts, concessions or commissions from the selling stockholders or commissions from purchasers of the shares of common stock for whom they may act as agent or to whom they may sell as principal. Such commissions will be in amounts to be negotiated, but, except as set forth in a supplement to this Prospectus, in the case of an agency transaction will not be in excess of a customary brokerage commission in compliance with FINRA Rule 2440; and in the case of a principal transaction a markup or markdown in compliance with FINRA IM-2440.

In connection with sales of the shares of common stock or otherwise, the selling stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the shares of common stock in the course of hedging in positions they assume. The selling stockholders may also sell shares of common stock short and if such short sale shall take place after the date that this Registration Statement is declared effective by the SEC, the selling stockholders may deliver shares of common stock covered by this prospectus to close out short positions and to return borrowed shares in connection with such short sales. The selling stockholders may also loan or pledge shares of common stock to broker-dealers that in turn may sell such shares, to the extent permitted by applicable law. The selling stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction). Notwithstanding the foregoing, the selling stockholders have been advised that they may not use shares registered on this registration statement to cover short sales of our common stock made prior to the date the registration statement, of which this prospectus forms a part, has been declared effective by the SEC.

The selling stockholders may, from time to time, pledge or grant a security interest in some or all of the shares of common stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of common stock from time to time pursuant to this prospectus or any amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act, amending, if necessary, the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus. The selling stockholders also may transfer and donate the shares of common stock in other circumstances in which case the transferees, donees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

The selling stockholders and any broker-dealer or agents participating in the distribution of the shares of common stock may be deemed to be “underwriters” within the meaning of Section 2(11) of the Securities Act in connection with such sales. In such event, any commissions paid, or any discounts or concessions allowed to, any such broker-dealer or agent and any profit on the resale of the shares purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. selling stockholders who are “underwriters” within the meaning of Section 2(11) of the Securities Act will be subject to the applicable prospectus delivery requirements of the Securities Act, including Rule 172 thereunder and may be subject to certain statutory liabilities of, including, but not limited to, Sections 11, 12 and 17 of the Securities Act and Rule 10b-5 under the Exchange Act.

Each selling stockholder has informed the Company that it is not a registered broker-dealer and does not have any written or oral agreement or understanding, directly or indirectly, with any person to distribute the common stock. Upon the Company being notified in writing by a selling stockholder that any material arrangement has been entered into with a broker-dealer for the sale of common stock through a block trade, special offering, exchange distribution or secondary distribution or a purchase by a broker or dealer, a supplement to this prospectus will be filed, if required, pursuant to Rule 424(b) under the Securities Act, disclosing (i) the name of each such selling stockholder and of the participating broker-dealer(s), (ii) the number of shares involved, (iii) the price at which such the shares of common stock were sold, (iv) the commissions paid or discounts or concessions allowed to such broker-dealer(s), where applicable, (v) that such broker-dealer(s) did not conduct any investigation to verify the information set out or incorporated by reference in this prospectus, and (vi) other facts material to the transaction. In no event shall any broker-dealer receive fees, commissions and markups, which, in the aggregate, would exceed eight percent (8.0%).

Under the securities laws of some states, the shares of common stock may be sold in such states only through registered or licensed brokers or dealers. In addition, in some states the shares of common stock may not be sold, unless such shares have been registered or qualified for sale in such state or an exemption from registration or qualification is available and is complied with.

There can be no assurance that any selling stockholder will sell any or all of the shares of common stock registered pursuant to the registration statement, of which this prospectus forms a part.

Each selling stockholder and any other person participating in such distribution will be subject to applicable provisions of the Exchange Act and the rules and regulations thereunder, including, without limitation, to the extent applicable, Regulation M of the Exchange Act, which may limit the timing of purchases and sales of any of the shares of common stock by the selling stockholder and any other participating person. To the extent applicable, Regulation M may also restrict the ability of any person engaged in the distribution of the shares of common stock to engage in market-making activities with respect to the shares of common stock. All of the foregoing may affect the marketability of the shares of common stock and the ability of any person or entity to engage in market-making activities with respect to the shares of common stock.

We will pay all expenses of the registration of the shares of common stock pursuant to the registration rights agreement, including, without limitation, SEC filing fees and expenses of compliance with state securities or "blue sky" laws; *provided, however*, that each selling stockholder will pay all underwriting discounts and selling commissions, if any and any related legal expenses incurred by it. We will indemnify the selling stockholders against certain liabilities, including some liabilities under the Securities Act, in accordance with the registration rights agreement, or the selling stockholders will be entitled to contribution. We may be indemnified by the selling stockholders against civil liabilities, including liabilities under the Securities Act, that may arise from any written information furnished to us by the selling stockholders specifically for use in this prospectus, in accordance with the related registration rights agreements, or we may be entitled to contribution.

LEGAL MATTERS

Unless otherwise indicated in any accompanying prospectus supplement, Skadden, Arps, Slate, Meagher & Flom LLP will provide opinions regarding the authorization and validity of the securities. Skadden, Arps, Slate, Meagher & Flom LLP may also provide opinions regarding certain other matters. Any underwriters will be advised about legal matters by their own counsel, which will be named in an accompanying prospectus supplement.

EXPERTS

The financial statements of Applied Therapeutics, Inc. appearing in Applied Therapeutics, Inc.'s [Annual Report \(Form 10-K\) for the year ended December 31, 2022](#) have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon (which contains an explanatory paragraph describing conditions that raise substantial doubt about the Company's ability to continue as a going concern as described in Note 1 to the financial statements), included therein, and incorporated herein by reference. Such financial statements are, and audited financial statements to be included in subsequently filed documents will be, incorporated herein in reliance upon the reports of Ernst & Young LLP pertaining to such financial statements (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.



\$300,000,000
Common Stock
Preferred Stock
Depository Shares
Debt Securities
Warrants
Offered by Applied Therapeutics, Inc.

Up to 38,250,000 Shares of Common Stock Issuable upon Exercise of Warrants

Up to 31,735,731 Shares of Common Stock for Resale
Offered by the Selling Stockholders

PROSPECTUS
