

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

**FORM S-3**  
REGISTRATION STATEMENT  
*UNDER*  
**THE SECURITIES ACT OF 1933**

**Applied Therapeutics, Inc.**  
(Exact name of registrant as specified in its charter)

**Delaware**  
(State or other jurisdiction of  
incorporation or organization)

**81-3405262**  
(I.R.S. Employer  
Identification Number)

**545 Fifth Avenue, Suite 1400**  
**New York, NY 10017**  
**(212) 220-9226**

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

**Shoshana Shendelman, Ph.D.**  
**President and Chief Executive Officer**  
**545 Fifth Avenue, Suite 1400**  
**New York, NY 10017**  
**(212) 220-9226**

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

**Copies to:**

**Michael J. Schwartz**  
**Skadden, Arps, Slate, Meagher & Flom LLP**  
**One Manhattan West**  
**New York, New York 10001**  
**Telephone: (212) 735-3000**  
**Facsimile: (212) 735-2000**

**Approximate date of commencement of proposed sale to the public:** From time to time after the effective date of this registration statement.

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

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

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

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

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

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

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

Large accelerated filer	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input checked="" type="checkbox"/>	Smaller reporting company	<input checked="" type="checkbox"/>
		Emerging growth company	<input checked="" type="checkbox"/>

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

**The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until we shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act or until the registration statement becomes effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.**

Subject to Completion, dated March 22, 2024

The information in this prospectus is not complete and may be changed. The selling stockholders may not sell these securities until the registration statement filed with the Securities and Exchange Commission is declared effective. This prospectus is not an offer to sell these securities and the selling stockholders are not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

## Preliminary Prospectus

## Applied Therapeutics, Inc.



## Up to 14,285,714 Shares of Common Stock

For Resale Offered by the Selling Stockholders

This prospectus relates to the disposition, from time to time, by the selling stockholders identified in this prospectus under the caption “Selling Stockholders” on page 7 of up to 14,285,714 shares of our common stock, par value \$0.0001 per share, or common stock, of which 2,000,000 shares are issuable upon the exercise of pre-funded warrants, with an exercise price of \$0.001 per warrant (the “Pre-Funded Warrants”), that we issued in a private placement completed on March 1, 2024 (the “Private Placement”).

The selling stockholders or their permitted transferees or other successors-in-interest may, but are not required to, sell the shares of our common stock offered by this prospectus from time to time in a number of different ways and at varying prices as determined by the prevailing market price for shares or in negotiated transactions. See “Plan of Distribution” on page 20 for a description of how the selling stockholders may dispose of the shares covered by this prospectus. We do not know when or in what amount the selling stockholders may offer the shares for sale.

We are not selling any shares of our common stock under this prospectus and 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 Pre-Funded Warrants, to the extent such Pre-Funded 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.

Our common stock is listed on The Nasdaq Global Market under the trading symbol “APLT.” On March 21, 2024, the last reported price of our common stock was \$6.82 per share.

*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.*

**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 \_\_\_\_\_, 2024

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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, the Selling Stockholders may offer and sell from time to time up to 14,285,714 shares of our common stock, of which 2,000,000 shares are issuable upon the exercise of the Pre-Funded Warrants. In some cases, the selling stockholders may also be required to provide a prospectus supplement containing specific information about the selling stockholders and the terms on which they are offering and selling our common stock. We may also add, update or change in a prospectus supplement or free writing prospectus information contained in this prospectus. You should read this prospectus and any accompanying prospectus supplement, and any documents incorporated by reference, as well as any post-effective amendments to the registration statement of which this prospectus is a part, before you make any investment decision. To the extent there is a conflict between the information contained in this prospectus and any applicable prospectus supplement, including the information incorporated by reference, you should rely on the information in the applicable prospectus supplement. 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.”

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 TM 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](http://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, 2023, filed with the SEC on March 6, 2024](#);
- the information specifically incorporated by reference into our [Annual Report on Form 10-K for the fiscal year ended December 31, 2023](#) from our definitive proxy statement on Schedule 14A, filed with the SEC on April 1, 2024;
- our Current Reports on Form 8-K, filed with the SEC on [January 3, 2024](#), [January 4, 2024](#), [February 15, 2024](#) and [February 29, 2024](#); 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, team, growth 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;
- 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](http://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 approximately \$2,000 from the exercise of all of the Pre-Funded Warrants, assuming the exercise in full of all of the Pre-Funded Warrants for cash.

Except as otherwise set forth in any accompanying prospectus supplement, we expect to use the net proceeds from the exercise of the Pre-Funded 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 14,285,714 shares of common stock of which, 2,000,000 shares are issuable upon the exercise the 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 Private Placement, without taking account of limitations on exercise of the selling stockholders’ existing warrants and Pre-Funded Warrants; (iii) the maximum number of shares that may be offered by each selling stockholder pursuant to this prospectus without taking account of limitations on exercise of the selling stockholders’ existing warrants and Pre-Funded 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, without taking into account limitations on exercise of the selling stockholders’ existing warrants and Pre-Funded Warrants.

Holders of Pre-Funded Warrants may not exercise any Pre-Funded 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. 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 105,886,831 shares of common stock outstanding as of March 5, 2024, which includes the 12,285,714 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 as of March 15, 2024. 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 <sup>(1)</sup>	Percentage of Outstanding Shares
Janus Henderson Biotech Innovation Master Fund Limited <sup>(2)</sup>	6,128,928	5.79%	2,574,286	3,554,642	3.36%
Janus Henderson Horizon Fund – Biotechnology Fund <sup>(2)</sup>	285,714	*	285,714	—	*
Perceptive Life Sciences Master Fund, Ltd. <sup>(3)</sup>	10,005,003	9.27%	2,860,000	7,145,003	6.75%
Tang Capital Partners, LP <sup>(4)</sup>	2,630,000	2.48%	1,430,000	1,200,000	1.13%
Alyeska Master Fund, LP <sup>(5)</sup>	5,489,226	5.00%	800,000	4,689,226	4.27%
Venrock Healthcare Capital Partners EG, L.P. <sup>(6)(7)</sup>	22,967,667	18.99%	1,087,229	21,880,438	18.09%
Venrock Healthcare Capital Partners III, L.P. <sup>(6)(7)</sup>	6,604,665	5.93%	311,597	6,293,068	5.65%
VHCP Co-Investment Holdings III, LLC <sup>(6)(7)</sup>	660,702	*	31,174	629,528	*
Adage Capital Partners L.P. <sup>(8)</sup>	2,649,784	2.50%	750,000	1,899,784	1.79%
Frazier Life Sciences Public Fund, L.P. <sup>(9)</sup>	919,392	*	718,432	200,960	*
Frazier Life Sciences Public Overage Fund, L.P. <sup>(10)</sup>	464,820	*	363,220	101,600	*
Frazier Life Sciences XI, L.P. <sup>(11)</sup>	283,833	*	221,793	62,040	*
Frazier Life Sciences X, L.P. <sup>(12)</sup>	161,955	*	126,555	35,400	*
Logos Global Master Fund LP <sup>(13)</sup>	750,000	0.71%	600,000	150,000	*
Entities Affiliated with Vestal Point Capital, LP <sup>(14)</sup>	5,105,000	4.82%	500,000	4,605,000	4.35%
Rock Springs Capital Master Fund LP <sup>(15)</sup>	1,620,000	1.53%	320,000	1,300,000	1.23%
Four Pines Master Fund LP <sup>(15)</sup>	257,918	*	60,000	197,918	*
Woodline Master Fund LP <sup>(16)</sup>	225,000	*	225,000	—	*
Octagon Investments Master Fund LP <sup>(17)</sup>	225,000	*	225,000	—	*
Catalio Public Equities Master Fund, LP <sup>(18)</sup>	344,205	*	170,714	173,491	*
StemPoint Capital Master Fund LP <sup>(19)</sup>	522,932	*	195,000	327,932	*
Titan Biotech Dislocation Fund SP <sup>(19)</sup>	385,834	*	30,000	355,834	*
GAKASA Holdings LLC <sup>(20)</sup>	5,799,687	5.48%	225,000	5,574,687	5.26%
Sphera Biotech Master Fund LP <sup>(21)</sup>	482,564	*	50,000	432,564	*
BEMAP Master Fund Ltd. <sup>(22)</sup>	104,855	*	4,211	100,644	*
Blackstone CSP-MST FMAP Fund <sup>(22)</sup>	104,856	*	4,211	100,645	*
Multi-Manager Access Vehicle LP <sup>(22)</sup>	88,552	*	3,559	84,993	*
Parkman HP Master Fund LP <sup>(22)</sup>	571,966	*	22,481	549,485	*
Schonfeld EXT Master Fund LP <sup>(23)</sup>	1,009,534	*	40,538	968,996	*
Laurion Capital Master Fund Ltd. <sup>(24)</sup>	1,481,006	1.40%	50,000	1,431,006	1.35%
<b>Total<sup>(25)</sup></b>	<b>78,330,598</b>	<b>70.60%</b>	<b>14,285,714</b>	<b>64,044,884</b>	<b>57.45%</b>

\* 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. The amount of Pre-Funded Warrants exercisable for shares of common stock held by each selling shareholder is subject to a beneficial ownership limitation of 9.99%.
- (2) Such shares may be deemed to be beneficially owned by Janus Henderson Investors US LLC (“Janus”), an investment adviser registered under the Investment Advisers Act of 1940, who acts as investment adviser for Janus Henderson Biotech Innovation Master Fund Limited (“JHBI Master Fund”) and Janus Henderson Horizon Fund — Biotechnology Fund (“JHH Biotechnology Fund” and together with the JHBI Master Fund, the “Janus Funds”) and has the ability to make decisions with respect to the voting and deposition of the shares subject to the oversight of the board of directors of the Janus Funds. Under the terms of its management contract with the Janus Funds, Janus has overall responsibility for directing the investments of the Janus Funds in accordance with the Janus Funds’ investment objective, policies and limitations. The Janus Funds have one or more portfolio managers appointed by and serving at the pleasure of Janus who make decisions with respect to the disposition of the shares of common stock offered hereby. The address for Janus is 151 Detroit Street, Denver, CO 80206. The portfolio managers for the Janus Funds are: Andrew Acker, Daniel S. Lyons and Agustin Mohedas.
- (3) Consists of (i) 8,005,003 shares and (ii) 2,000,000 shares issuable upon the exercise of the Pre-Funded Warrants. Perceptive Advisors LLC is the investment advisor of Perceptive Life Sciences Master Fund, Ltd. (“Perceptive Fund”). Joseph Edelman is the controlling person of Perceptive Fund. Mr. Edelman disclaims beneficial ownership of such shares except to the extent of his pecuniary interest therein. The address of the aforementioned entities and individual is 51 Astor Place, 10<sup>th</sup> Floor, New York, NY 10003.
- (4) Kevin Tang is the sole manager of Tang Capital Management, LLC, which is the general partner of Tang Capital Partners, LP. Accordingly, Mr. Tang may be deemed to have beneficial ownership of the shares beneficially owned by Tang Capital Partners, LP. Mr. Tang has a pecuniary interest in the shares beneficially held by Tang Capital Partners, LP. The address of the aforementioned entities and individual is 4747 Executive Drive, Suite 210, San Diego, CA 92121.
- (5) Consists of (i) 1,489,226 shares and (ii) 4,000,000 shares issuable upon exercise of common warrants obtained in the Company’s private placement that closed on June 27, 2022 (“2022 Common Warrants”). Alyeska Investment Group, L.P. (“Alyeska LP”) is the investment manager of Alyeska Master Fund, L.P. (“Alyeska Master Fund”) and has voting and investment control of the shares held by Alyeska Master Fund. Anand Parekh is the Chief Executive Officer of Alyeska LP. Accordingly, Alyeska LP and Mr. Parekh may be deemed to have beneficial ownership of the shares beneficially owned by Alyeska Master Fund. Mr. Parekh disclaims any beneficial ownership of such shares except to the extent of his pecuniary interest therein. The address of Alyeska Master Fund, L.P. is c/o Maples Corporate Services Limited, P.O. Box 309, Uglund House, South Church Street George Town, Grand Cayman, KY1-1104, Cayman Islands. Alyeska Investment Group, L.P. is located at 77 W. Wacker, Suite 700, Chicago IL 60601.
- (6) 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 aforementioned entities is 7 Bryant Park, 23rd Floor, New York, NY 10018.
- (7) Consists of: (i) 7,928,536 shares and 15,039,131 shares issuable upon the exercise of the pre-funded warrants obtained in the Company’s private placement that closed on April 26, 2023 (“2023 Pre-Funded Warrants”) held by VHCP EG; (ii) 1,042,218 shares and 5,562,447 shares issuable upon the exercise of the 2023 Pre-Funded Warrants held by VHCP III; and (iii) 104,246 shares and 556,456 shares issuable upon exercise of the 2023 Pre-Funded Warrants held by VHCP Co-III.
- (8) Adage Capital Advisors, L.L.C. (“Adage Capital Advisors”) is the managing member of Adage Capital Partners GP, L.L.C., which is the general partner of Adage Capital Partners L.P. Bob Atchinson and Phillip Gross are the managing members of Adage Capital Advisors. Messrs. Atchinson and Gross disclaim beneficial ownership of such shares except to the extent of their respective pecuniary interest therein. The address of the aforementioned entities and individuals is 200 Clarendon Street, 52<sup>nd</sup> Floor, Boston, MA 02116.
- (9) FHMLSP, L.P. is the general partner of Frazier Life Sciences Public Fund, L.P. (“FLS PF”) and

- FHMLSP, L.L.C. is the general partner of FHMLSP, L.P. Albert Cha, James N. Topper, Patrick J. Heron and James Brush are the managing directors of FHMLSP, L.L.C. and therefore share voting and investment power over the shares held by FLS PF. Dr. Cha, Dr. Topper, Mr. Heron and Dr. Brush disclaim beneficial ownership of the shares held by FLS PF except to the extent of their pecuniary interests in such shares, if any. The address of the aforementioned entities and individuals is 1001 Page Mill Road, Building 4, Suite B, Palo Alto, CA 94304.
- (10) FHMLSP Overage, L.P. is the general partner of Frazier Life Sciences Public Overage Fund, L.P. (“FLS POF”) and FHMLSP Overage, L.L.C. is the general partner of FHMLSP Overage, L.P. Dr. Cha, Dr. Topper, Mr. Heron and Dr. Brush are the members of FHMLSP Overage, L.L.C. and therefore share voting and investment power over the shares held by FLS POF. Dr. Cha, Dr. Topper, Mr. Heron and Dr. Brush disclaim beneficial ownership of the shares held by FLS POF except to the extent of their pecuniary interests in such shares, if any. The address of the aforementioned entities and individuals is 1001 Page Mill Road, Building 4, Suite B, Palo Alto, CA 94304.
- (11) FHMLS XI, L.P. is the general partner of Frazier Life Sciences XI, L.P. (“FLS XI”), and FHMLS XI, L.L.C. is the general partner of FHMLS XI, L.P. Mr. Heron, Dr. Topper and Daniel Estes are the members of FHMLS XI, L.L.C. and therefore share voting and investment power over the shares held by FLS XI. Dr. Topper, Mr. Heron and Mr. Estes disclaim beneficial ownership of the shares held by FLS XI except to the extent of their pecuniary interests in such shares, if any. The address of the aforementioned entities and individuals is 1001 Page Mill Road, Building 4, Suite B, Palo Alto, CA 94304.
- (12) FHMLS X, L.P. is the general partner of Frazier Life Sciences X, L.P. (“FLS X”), and FHMLS X, L.L.C. is the general partner of FHMLS X, L.P. Mr. Heron and Dr. Topper are the members of FHMLS X, L.L.C. and therefore share voting and investment power over the shares held by FLS X. Dr. Topper and Mr. Heron disclaim beneficial ownership of the shares held by FLS X except to the extent of their pecuniary interests in such shares, if any. The address of the aforementioned entities and individuals is 1001 Page Mill Road, Building 4, Suite B, Palo Alto, CA 94304.
- (13) Logos Global Management LP (“Logos Global”) is the investment advisor to Logos Global Master Fund LP (“Logos Fund”). Logos Global Management GP LLC (“Logos Global GP”) is the general partner of Logos Global. Arsani William is a controlling person of Logos Global and Logos Global GP and may be deemed to have beneficial ownership of the shares beneficially owned by Logos Fund. Mr. William disclaims beneficial ownership of such shares except to the extent of his pecuniary interest therein. The address of the entities listed above is 1 Letterman Drive, C3-350, San Francisco, CA 94129.
- (14) Consists of: (i) 2,152,890 shares held by Vestal Point Master Fund, LP and (ii) 2,452,110 shares held by an account separately managed by Vestal Point Capital, LP. The sole general partner of Vestal Point Master Fund, LP is Vestal Point Partners GP, LLC. The managing member of Vestal Point Partners GP, LLC is Ryan Wilder. The sole general partner of Vestal Point Capital, LP is Vestal Point Capital, LLC. The managing member of Vestal Point Capital, LLC is Mr. Wilder. As a result, Mr. Wilder may be deemed to have voting and investment power over the securities held by Vestal Point Master Fund, LP and the account separately managed by Vestal Point Capital, LP. Mr. Wilder disclaims beneficial ownership of such securities, except to the extent of his pecuniary interest therein. The address of these entities and Mr. Wilder is c/o Vestal Point Capital, LP, 632 Broadway, Suite 602, New York, NY 10012.
- (15) Rock Springs Capital Management LP. (“RSCM”) is the investment manager of Rock Springs Capital Master Fund LP. (“Rock Springs Fund”) and Four Pines Master Fund LP (“Four Pines Fund”). The general partner of RSCM is Rock Springs Capital LLC (“RSC”). RSC and RSCM may therefore be deemed to have or share beneficial ownership of the shares held directly by the Rock Springs Fund and Four Pines Fund. The address for RSC and RSCM is 650 South Exeter St., Suite 1070, Baltimore, Maryland 21202.
- (16) Woodline Partners LP serves as the investment manager of Woodline Master Fund LP. Accordingly, Woodline LP may be deemed to have beneficial ownership of the shares beneficially owned by Woodline Master Fund LP. Woodline Partners LP disclaims any beneficial ownership of these shares. The address of Woodline Master Fund LP is 4 Embarcadero Center, Suite 3450, San Francisco, CA 94111.
- (17) Octagon Capital Advisors LP (“Octagon Advisors”) is the investment manager of Octagon Investments Master Fund LP. Ting Jia, Ph.D. is the Founder, Managing Member and Chief Investment Officer of

- Octagon Advisors. By virtue of such relationships, Dr. Jia and Octagon Advisors may be deemed to have voting and investment power of the shares held by Octagon Investments Master Fund LP. Each of Dr. Jia and Octagon Capital Advisors LP disclaims beneficial ownership of the shares held by Octagon Investments Master Fund LP, except to the extent of his or its pecuniary interest therein, if any. The address for each of Dr. Jia, Octagon Capital Advisors LP and Octagon Investments Master Fund LP is 654 Madison Avenue, 21st Floor, New York, NY 10065.
- (18) George Petrocheilos and R. Jacob Vogelstein hold voting and investment control of the shares held by Catalio Public Equities Master Fund, LP. Mr. Petrocheilos and Mr. Vogelstein disclaim beneficial ownership over such shares, except to the extent of their pecuniary interest therein. The address of the aforementioned entities and individuals is 512 West 22<sup>nd</sup> Street, 5<sup>th</sup> Floor, New York, NY 10011.
- (19) StemPoint Capital LP (“StemPoint”) serves as investment advisor to StemPoint Capital Master Fund LP (“StemPoint Fund”) and as sub-advisor to Titan Biotech Dislocation Fund SP (“TBDF”). StemPoint exercises voting and investment power over the shares held by StemPoint Fund pursuant to investment management agreements and StemPoint exercises investment power over the shares held by TBDF pursuant to its sub-advisory agreement. Michelle Ross and Sean Tan are members of the Investment Manager of StemPoint. Accordingly, StemPoint, Ms. Ross and Mr. Tan may be deemed to have beneficial ownership of the shares beneficially owned by StemPoint Fund and TBDF. StemPoint, Ms. Ross and Mr. Tan disclaim beneficial ownership of the shares held by StemPoint Fund and TBDF, except to the extent of their pecuniary interest therein. The address of StemPoint Fund is 520 Madison Ave, 19<sup>th</sup> Floor, New York, NY 10022. The address of TBDF is 750 Washington Blvd, 10<sup>th</sup> Floor, Stamford, CT 06901.
- (20) Knoll Capital Management LLC, holds voting and investment power over the shares held by GAKASA Holdings LLC. Fred Knoll is the President of Knoll Capital Management. GAKASA Holdings is owned 100% by the Knoll Family Trust. Fred Knoll is a beneficiary of the Trust. The address of the aforementioned entities and individuals is 17749 Collins Ave PH45, Sunny Isles, FL 33160.
- (21) Sphera Biotech GP LP (the “Sphera General Partner”) is the general partner of Sphera Biotech Master Fund LP. Sphera Global Healthcare Management LP is the general partner of the Sphera General Partner and acts as the Investment Manager for Sphera Biotech Master Fund and holds voting and investment power over the shares held by Sphera Biotech Master Fund. Accordingly, Sphera Global Healthcare Management LP may be deemed to have beneficial ownership of the shares held by Sphera Biotech Master Fund LP. Sphera Global Healthcare Management LP disclaims beneficial ownership of such shares, except to the extent of its pecuniary interest therein. The address of the aforementioned entities is 4 Yitzhak Sadeh, Entrance A, 29<sup>th</sup> Floor, Tel Aviv 6777520 Israel.
- (22) Parkman Healthcare Partners LLC (“Parkman LLC”) holds voting and investment power over the shares held by BEMAP Master Fund Ltd., Blackstone CSP-MST FMAP Fund and Multi-Manager Access Vehicle LP. Gregory Martinez is the managing member of Parkman LLC and holds voting and investment power over the shares held by Parkman HP Master Fund LP. Mr. Martinez disclaims any beneficial ownership of such shares except to the extent of his pecuniary interest therein. The address of the aforementioned entities and individual is 700 Canal Street, 2<sup>nd</sup> Floor, Stamford CT 06906.
- (23) Schonfeld Strategic Advisors LLC (“Schonfeld LLC”) holds voting and investment power over the shares held by Schonfeld EXT Master Fund LP. Accordingly, Schonfeld LLC may be deemed to have beneficial ownership of the shares held by Schonfeld EXT Master Fund LP. Schonfeld LLC disclaims any beneficial ownership of such shares except to the extent of their pecuniary interest therein. The address of the aforementioned entities is 590 Madison Ave, Floor 23, New York, NY 10022.
- (24) Laurion Capital Management LP, the investment manager of Laurion Capital Master Fund Ltd., has voting and investment power over the securities held by Laurion Capital Master Fund Ltd. Messrs. Benjamin A. Smith and Sheehan Maduraperuma are the managing members of Laurion Capital GP LLC, which is the general partner of Laurion Capital Management LP. Each of Laurion Capital Master Fund Ltd., Laurion Capital GP LLC, Benjamin A. Smith and Sheehan Maduraperuma disclaims beneficial ownership over these securities. The address of the aforementioned entities is 360 Madison Avenue, Suite 1900, New York, NY 10017.
- (25) The number of shares beneficially owned after this offering consists of (i) 38,886,850 shares and (ii) 25,158,034 shares issuable upon the exercise of 4,000,000 2022 Common Warrants and 21,158,034 2023 Pre-Funded Warrants.

## DESCRIPTION OF SECURITIES

This prospectus contains summary descriptions of the common stock 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 March 5, 2024, 105,886,831 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 (66-2/3%)) 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 (66-2/3%) 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 Pre-Funded Warrants in the Private Placement are entitled to certain rights with respect to registration of such shares of common stock and shares issuable upon exercise of the 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 February 27, 2024 (the “Registration Rights Agreement”). The registration of shares of our common stock and shares issuable upon exercise of the 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 (66-2/3%) 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 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

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, 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 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.





**Up to 14,285,714 Shares of Common Stock**

**For Resale Offered by the Selling Stockholders**

**PRELIMINARY PROSPECTUS**

**, 2024**

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## PART II INFORMATION NOT REQUIRED IN PROSPECTUS

**Item 14. Other Expenses of Issuance and Distribution.**

The following table sets forth the costs and expenses, payable by the registrant in connection with the sale of our common stock being registered. All amounts are estimates except for the SEC registration fee and the Financial Industry Regulatory Authority, or FINRA, filing fee.

Securities and Exchange Commission Registration Fee	\$ 13,874.40
FINRA Filing Fee	45,500
Accounting Fees and Expenses	15,000
Legal Fees and Expenses	75,000
Printing Fees	12,000
Transfer Agents and Trustees' Fees and Expenses	20,000
Miscellaneous	0
Total	<u>\$181,374.40</u>

**Item 15. Indemnification of Directors and Officers.**

As permitted by Section 102 of the General Corporation Law of the State of Delaware (the "DGCL"), we have adopted provisions in our amended and restated certificate of incorporation and amended and restated bylaws that limit or eliminate the personal liability of our directors for a breach of their fiduciary duty of care as a director. The duty of care generally requires that, when acting on behalf of the corporation, directors exercise an informed business judgment based on all material information reasonably available to them. Consequently, a director will not be personally liable to us or our stockholders for monetary damages for breach of fiduciary duty as a director, except for liability for:

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

These limitations of liability do not affect the availability of equitable remedies such as injunctive relief or rescission. Our amended and restated certificate of incorporation also authorizes us to indemnify our officers, directors and other agents to the fullest extent permitted under Delaware law.

As permitted by Section 145 of the DGCL, our amended and restated bylaws provide that:

- we may indemnify our directors, officers and employees to the fullest extent permitted by the DGCL, subject to limited exceptions;
- we may advance expenses to our directors, officers and employees in connection with a legal proceeding to the fullest extent permitted by the DGCL, subject to limited exceptions; and
- the rights provided in our amended and restated bylaws are not exclusive.

Our amended and restated certificate of incorporation and our amended and restated bylaws provide for the indemnification provisions described above and elsewhere herein. We have entered or will enter into, and intend to continue to enter into, separate indemnification agreements with our directors and officers that may be broader than the specific indemnification provisions contained in the DGCL. These indemnification agreements generally require us, among other things, to indemnify our officers and directors against liabilities that may arise by reason of their status or service as directors or officers, other than liabilities arising from willful misconduct. These indemnification agreements also generally require us to advance any expenses incurred by the directors or officers as a result of any proceeding against them as to

which they could be indemnified. These indemnification provisions and the indemnification agreements may be sufficiently broad to permit indemnification of our officers and directors for liabilities, including reimbursement of expenses incurred, arising under the Securities Act.

The registrant has purchased and currently intends to maintain insurance on behalf of each and every person who is or was a director or officer of the registrant against any loss arising from any claim asserted against him or her and incurred by him or her in any such capacity, subject to certain exclusions.

#### Item 16. List of Exhibits.

Exhibit No.	Description
1.1*	Form of Underwriting Agreement.
4.1	<a href="#">Registration Rights Agreement, dated April 23, 2023, by and among the Company and the Purchasers named therein (incorporated by reference to Exhibit 10.2 to the registrant's Current Report on Form 8-K filed on April 24, 2023).</a>
4.2	<a href="#">Registration Rights Agreement, dated February 27, 2024, by and among the Company and the Purchasers named therein (incorporated by reference to Exhibit 10.2 to the registrant's Current Report on Form 8-K filed on March 1, 2024).</a>
4.3	<a href="#">Form of Common Stock Certificate (incorporated by reference to Exhibit 4.1 to the registrant's Quarterly Report on Form 10-Q filed August 12, 2019).</a>
4.4	<a href="#">Form of Warrant, issued to affiliates of Brookline Capital Markets, a division of CIM Securities LLC, on March 13, 2017 (incorporated by reference to Exhibit 4.3 to the registrant's Registration Statement on Form S-1/A filed on April 29, 2019).</a>
4.5	<a href="#">Form of Warrant, issued to affiliates of Brookline Capital Markets, a division of CIM Securities LLC, on November 5, 2018 (incorporated by reference to Exhibit 4.4 to the registrant's Registration Statement on Form S-1/A filed on April 29, 2019).</a>
4.6	<a href="#">Form of Warrant, issued to affiliates of Brookline Capital Markets, a division of CIM Securities LLC, on April 9, 2019 (incorporated by reference to Exhibit 4.5 to the registrant's Registration Statement on Form S-1/A filed on April 29, 2019).</a>
4.7	<a href="#">Amendment No. 1 to Form of Common Stock Purchase Warrant (incorporated by reference to Exhibit 4.1 of the registrant's Quarterly Report on Form 10-Q filed May 11, 2023).</a>
4.8	<a href="#">Form of 2022 Common Warrant to Purchase Common Stock (incorporated by reference to Exhibit 4.2 of the registrant's Current Report on Form 8-K filed June 27, 2022).</a>
4.9	<a href="#">Form of 2023 Pre-Funded Common Stock Purchase Warrant (incorporated by reference to Exhibit 4.1 of the registrant's Current Report on Form 8-K filed April 27, 2023).</a>
4.10	<a href="#">Form of 2024 Pre-Funded Common Stock Purchase Warrant (incorporated by reference to Exhibit 4.1 of the registrant's Current Report on Form 8-K filed March 1, 2024).</a>
5.1	<a href="#">Opinion of Skadden, Arps, Slate, Meagher &amp; Flom LLP.</a>
23.1	<a href="#">Consent of Ernst &amp; Young LLP, Independent Registered Public Accounting Firm.</a>
23.2	<a href="#">Consent of Skadden, Arps, Slate, Meagher &amp; Flom LLP (included in Exhibit 5.1).</a>
24.1	<a href="#">Powers of Attorney (included on signature pages hereto).</a>
107	<a href="#">Filing Fee Table</a>

\* To be filed by amendment to the Registration Statement or incorporated by reference from documents filed or to be filed with the SEC under the Securities Exchange Act of 1934, as amended.

#### Item 17. Undertakings.

The undersigned registrant hereby undertakes:

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

- (i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;
- (ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the SEC pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement;
- (iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

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

- (2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
- (3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.
- (4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:
  - (i) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of this registration statement as of the date the filed prospectus was deemed part of and included in this registration statement; and
  - (ii) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii) or (x) for the purpose of providing the information required by section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in this registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof. Provided, however, that no statement made in a registration statement or prospectus that is part of this registration statement or made in a document incorporated or deemed incorporated by reference into this registration statement or prospectus that is part of this registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in this registration statement or prospectus that was part of this registration statement or made in any such document immediately prior to such effective date.
- (5) That, for the purpose of determining liability of the registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities, the undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the

securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

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

The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of the Company's jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

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



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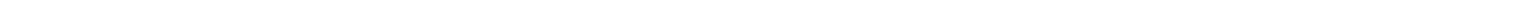
March 22, 2024

Applied Therapeutics, Inc.  
545 Fifth Avenue, Suite 1400  
New York, New York 10017

Re: Applied Therapeutics, Inc.  
Registration Statement on Form S-3

Ladies and Gentlemen:

We have acted as special United States counsel to Applied Therapeutics, Inc., a Delaware corporation (the "Company"), in connection with the registration for resale under the Securities Act of 1933 (the "Securities Act"), of an aggregate of 14,285,714 shares of the Company's common stock, par value \$0.0001 per share, consisting of (i) 12,285,714 shares (the "Existing Secondary Shares") and (ii) 2,000,000 shares (the "Warrant Secondary Shares" and, together with the Existing Secondary Shares the "Secondary Shares") issuable upon the exercise of 2,000,000 pre-funded warrants, with an exercise price of \$0.001 per pre-funded warrant (the "Pre-Funded Warrants"), on behalf of the Selling Stockholders (as defined herein). We have been advised that the Existing Secondary Shares and the Pre-Funded Warrants were issued pursuant to a Securities Purchase Agreement (the "Securities Purchase Agreement"), dated February 27, 2024, by and among the Company and the selling stockholders named therein (the "Selling Stockholders").



This opinion is being furnished in accordance with the requirements of Item 601(b)(5) of Regulation S-K under the Securities Act.

In rendering the opinions stated herein, we have examined and relied upon the following:

- (a) the registration statement on Form S-3 (the "Registration Statement") to be filed on the date hereof by the Company relating to the Secondary Shares with the Securities and Exchange Commission (the "Commission") under the Securities Act;
  - (b) the prospectus, which forms a part of and is included in the Registration Statement;
  - (c) an executed copy of the Securities Purchase Agreement;
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(d) an executed copy of a certificate of Shoshana Shendelman, Secretary of the Company, dated the date hereof (the “Secretary’s Certificate”);

(e) a copy of the Company’s Amended and Restated Certificate of Incorporation as certified by the Secretary of State of the State of Delaware as of March 21, 2024, and certified pursuant to the Secretary’s Certificate (the “Amended and Restated Certificate of Incorporation”);

(f) a copy of the Company’s Amended and Restated Certificate of Incorporation, as in effect as of the date the Existing Secondary Shares were issued, and certified pursuant to the Secretary’s Certificate (the “Prior Amended and Restated Certificate of Incorporation”);

(g) a copy of the Company’s Amended and Restated Bylaws, as in effect as of the date hereof and certified pursuant to the Secretary’s Certificate (the “Amended and Restated Bylaws”);

(h) a copy of the Company’s Amended and Restated Bylaws, as in effect as of the date the Existing Secondary Shares were issued, and certified pursuant to the Secretary’s Certificate (the “Prior Amended and Restated Bylaws”);

(i) a copy of certain resolutions of the Board of Directors of the Company, adopted on February 26, 2024 and certain resolutions of the Pricing Committee thereof, adopted on February 27, 2024, each certified pursuant to the Secretary’s Certificate; and

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- (j) executed copies of the Pre-Funded Warrants.

We have also examined originals or copies, certified or otherwise identified to our satisfaction, of such records of the Company and such agreements, certificates and receipts of public officials, certificates of officers or other representatives of the Company and others, and such other documents as we have deemed necessary or appropriate as a basis for the opinions stated below, including the facts and conclusions set forth in the Secretary's Certificate.

In our examination, we have assumed the genuineness of all signatures, including electronic signatures, the legal capacity and competency of all natural persons, the authenticity of all documents submitted to us as originals, the conformity to original documents of all documents submitted to us as facsimile, electronic, certified or photocopied copies, and the authenticity of the originals of such copies. With respect to our opinions set forth below, we have assumed that (i) the Company received in full the consideration for the Secondary Shares set forth in the Securities Purchase Agreement and the Pre-Funded Warrants, as applicable and the applicable resolutions of the Board of Directors of the Company approving the issuance of all such Secondary Shares, (ii) the issuance of the Existing Secondary Shares has been and the issuance of the Warrant Secondary Shares will be registered in the Company's share registry, and (iii) the issuance of the Warrant Secondary Shares does not and the issuance of the Existing Secondary Shares did not violate or conflict with any agreement or instrument binding on the Company (except that we do not make this assumption with respect to (i) in the case of the Warrant Secondary Shares, the Amended and Restated Certificate of Incorporation and the Amended and Restated Bylaws, and (ii) in the case of the Existing Secondary Shares, the Prior Amended and Restated Certificate of Incorporation and the Prior Amended and Restated Bylaws, and in either case, those agreements or instruments expressed to be governed by the laws of the State of New York which are listed in the Company's Annual Report on Form 10-K for the year ended December 31, 2023). As to any facts relevant to the opinions stated herein that we did not independently establish or verify, we have relied upon statements and representations of officers and other representatives of the Company and the Selling Stockholders and others and of public officials, including the facts and conclusions set forth in the Secretary's Certificate and the factual representations and warranties set forth in the Securities Purchase Agreement.

We do not express any opinion with respect to the laws of any jurisdiction other than the General Corporation Law of the State of Delaware (the "DGCL").

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Based upon the foregoing and subject to the qualifications and assumptions stated herein, we are of the opinion that:

1. the Warrant Secondary Shares being sold by the Selling Stockholders have been duly authorized by all requisite corporate action on the part of the Company under the DGCL and when issued in accordance with the terms of the Pre-Funded Warrants by the Company against payment of the exercise price therefor and registered in the Company's share registry will be validly issued and fully paid and nonassessable; and

2. the Existing Secondary Shares being sold by the Selling Stockholders have been duly authorized by all requisite corporate action on the part of the Company under the DGCL and are validly issued and fully paid and nonassessable.

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Applied Therapeutics, Inc.

March 22, 2024

Page 6

We hereby consent to the reference to our firm under the heading "Legal Matters" in the prospectus forming part of the Registration Statement. We also hereby consent to the filing of this opinion with the Commission as an exhibit to the Registration Statement. In giving this consent, we do not thereby admit that we are within the category of persons whose consent is required under Section 7 of the Securities Act or the general Rules and Regulations under the Securities Act. This opinion is expressed as of the date hereof unless otherwise expressly stated, and we disclaim any undertaking to advise you of any subsequent changes in the facts stated or assumed herein or of any subsequent changes in applicable laws.

Very truly yours,

/s/ Skadden, Arps, Slate Meagher & Flom LLP

MJS

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**Consent of Independent Registered Public Accounting Firm**

We consent to the reference to our firm under the caption "Experts" in the Registration Statement (Form S-3) and related Prospectus of Applied Therapeutics, Inc. for the registration of 14,285,714 shares of its common stock and to the incorporation by reference therein of our report dated March 6, 2024, with respect to the financial statements of Applied Therapeutics, Inc., included in its Annual Report (Form 10-K) for the year ended December 31, 2023, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

New York, New York  
March 22, 2024

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## Calculation of Filing Fee Table

Form S-3

(Form Type)

## APPLIED THERAPEUTICS, INC.

(Exact Name of Registrant as Specified in its Charter)

**Table 1 - Newly Registered Securities**

	Security Type	Security Class Title	Fee Calculation or Carry Forward Rule	Amount Registered	Proposed Maximum Offering Price Per Share	Maximum Aggregate Offering Price	Fee Rate	Amount of Registration Fee
Fees to Be Paid	Equity	Common Stock, par value \$0.0001 per share, offered by the selling stockholders <sup>(1)</sup>	457(a) 457(c)	14,285,714	\$5.86 <sup>(2)</sup>	\$83,714,284.04 <sup>(2)</sup>	\$0.00014760	\$12,356.23
Total				14,285,714		\$83,714,284.04		\$12,356.23

(1) Pursuant to Rule 416 under the Securities Act of 1933, as amended (the "Securities Act"), the shares of common stock being registered hereunder include an indeterminate number of shares that may be issued in connection with shares splits, share dividends, recapitalizations or similar events.

(2) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(c) under the Securities Act based on the average high and low sale price for the common shares on March 15, 2024 as reported on Bloomberg.