

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

**Post-Effective Amendment No. 2
to**

**FORM S-1
on 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)

2834
(Primary Standard Industrial
Classification Code Number)
545 Fifth Avenue, Suite 1400
New York, NY 10017
(212) 220-9226

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

(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:

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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

Non-accelerated filer

Accelerated filer

Smaller reporting company

Emerging growth company

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

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.

EXPLANATORY NOTE

On December 13, 2019, Applied Therapeutics, Inc. (the "Company") filed a registration statement with the Securities and Exchange Commission (the "SEC") on Form S-1 (Registration No. 333-235504), which was amended by Pre-Effective Amendment No. 1 filed with the SEC on December 19, 2020 (as amended, the "Form S-1"). The Form S-1 was declared effective by the SEC on December 20, 2019 and registers for resale by the selling shareholders named in the prospectus up to 1,380,344 shares of common stock of the Company, par value \$0.0001 per share (the "common stock"). On March 13, 2020, the Company filed Post-Effective Amendment No. 1 to the Form S-1 to update the prospectus to include the information contained in the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2019 that was filed with the SEC on March 13, 2020 ("Post-Effective Amendment No. 1"). Post-Effective Amendment No. 1 was declared effective by the SEC on March 23, 2020.

This Post-Effective Amendment No. 2 to Form S-1 on Form S-3 ("Post-Effective Amendment No. 2") is being filed by the Company (i) to convert the Form S-1 into a registration statement on Form S-3 and (ii) to include an updated prospectus relating to the offering and sale of the shares that were registered for resale on the Form S-1.

No additional securities are being registered under this Post-Effective Amendment No. 2. All applicable registration fees were paid at the time of the original filing of the Registration Statement.

Subject to Completion, dated June 4, 2020

Preliminary Prospectus

Applied Therapeutics, Inc.



1,380,344 Shares of Common Stock

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 8 of up to 1,380,344 shares of our common stock, par value \$0.0001 per share, or common stock.

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 10 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. 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 "ALPT." On June 3, 2020, the last reported price of our common stock was \$44.00 per share.

Investing in our common stock involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading "Risk Factors" starting on page 7 of this prospectus and other risk factors contained in the documents incorporated by reference herein.

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 _____, 2020

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.

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

We have not authorized anyone to provide any information or to make any representations other than those contained in this prospectus or in any free writing prospectuses prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus is an offer to sell only the shares offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus or in any applicable free writing prospectus is current only as of its date, regardless of its time of delivery or any sale of shares of our common stock. Our business, financial condition, results of operations and prospects may have changed since that date.

We have not done anything that would permit this offering or possession or distribution of this prospectus or any free writing prospectus in any jurisdiction where action for that purpose is required, other than in the United States. You are required to inform yourself about and to observe any restrictions relating as to this offering and the distribution of this prospectus and any such free writing prospectus outside the United States.

ABOUT THIS PROSPECTUS

This prospectus is part of a resale registration statement that we filed with the Securities and Exchange Commission (the "SEC") using a "shelf" registration process. The selling stockholders may offer and sell, from time to time, an aggregate of up to 1,380,344 shares of our common stock under this prospectus. In some cases, we and the selling stockholders will 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 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.

You should rely only on the information contained in this prospectus and any accompanying prospectus supplement, including the information incorporated by reference herein. Neither we nor the selling stockholders have authorized anyone to provide you with information different from that contained in this prospectus or any accompanying prospectus supplement, including the information incorporated by reference herein.

The selling stockholders may only offer to sell, and seek offers to buy, our common stock in jurisdictions where offers and sales are permitted. The information contained in this prospectus speaks only as of the date of this prospectus.

WHERE YOU CAN FIND MORE INFORMATION

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

The SEC allows us to "incorporate by reference" information into this prospectus and any accompanying prospectus supplement, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus and any accompanying prospectus supplement, except for any information superseded by information contained directly in this prospectus, any accompanying prospectus supplement, any subsequently filed document deemed incorporated by reference or any free writing prospectus prepared by or on behalf of us. This prospectus and any accompanying prospectus supplement incorporate by reference the documents set forth below that we have previously filed with the SEC (other than information deemed furnished and not filed in accordance with SEC rules, including Items 2.02 and 7.01 of Form 8-K).

- [our Annual Report on Form 10-K for the fiscal year ended December 31, 2019, filed with the SEC on March 13, 2020;](#)
- the information specifically incorporated by reference into our Annual Report on Form 10-K for the fiscal year ended [December 31, 2019](#) from our definitive proxy statement on Schedule 14A, filed with the SEC on [April 23, 2020](#);
- our Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2020, filed with the SEC on [May 11, 2020](#);
- our Current Reports on Form 8-K, filed with the SEC on [February 14, 2020](#), [April 1, 2020](#), [April 21, 2020](#) (only with respect to Item 8.01) and [May 26, 2020](#); 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.](#)

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 Post-Effective Amendment No. 2 of which this prospectus is a part and prior to effectiveness of the Post-Effective Amendment No. 2 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.

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 facts 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," "goal," "intend," "may," "objective," "plan," "predict," "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:

- the potential impact of the Covid-19 pandemic on the timing and progress of our ongoing clinical trials, our business, results of operations, liquidity, and operations and our ability to mitigate those potential impacts;
- our plans to develop and commercialize our product candidates;
- the initiation, timing, progress and results of our current and future preclinical studies and clinical trials and our research and development programs;
- our ability to take advantage of expedited regulatory pathways for any of our product candidates;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our ability to successfully acquire or in-license additional product candidates on reasonable terms;
- our ability to maintain and establish collaborations or obtain additional funding;
- our ability to obtain regulatory approval of our current and future product candidates;
- 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.

PROSPECTUS SUMMARY**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 potential use of expedited 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 pediatric metabolic diseases. Using similar strategies to our AR inhibitors, or ARI, program, we have also developed a program targeting selective inhibition of phosphatidylinositol 3-kinase, or PI3K, subunits that produced an early-stage oncology pipeline. 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. We plan to initiate our clinical program in these indications in 2021.

November 2019 Private Placement

On November 7, 2019, we entered into a securities purchase agreement for a private placement (the "Private Placement") with a select group of accredited investors, which we collectively refer to as the Purchasers. Pursuant to the securities purchase agreement, the Purchasers purchased 1,380,344 shares of our common stock. The purchase price for each share was \$14.50, with net proceeds of approximately \$18 million. The closing of the purchase and sale of the securities occurred on November 12, 2019.

We also entered into a registration rights agreement with the Purchasers requiring us to register the resale of the Shares. Pursuant to such registration rights agreement, we prepared and filed the Form S-1.

THE OFFERING

Common stock to be offered	1,380,344 shares
Common stock to be outstanding after this offering	22,126,772 shares
Use of proceeds	We will not receive any proceeds from the sale of shares in this offering. See the sections titled "Use of Proceeds" and "Selling Stockholders" for additional information.
Risk factors	You should read the section titled "Risk Factors" for a discussion of factors to consider carefully, together with all the other information included in this prospectus, before deciding to invest in our common stock.
Nasdaq Global Market symbol	"APLT"

The number of shares of our common stock to be outstanding after this offering is based on 22,126,772 shares of common stock outstanding as of June 1, 2020, and excludes:

- options to purchase 3,948,090 shares of common stock outstanding under the 2016 Equity Incentive Plan (the "2016 Plan") and the 2019 Equity Incentive Plan (the "2019 Plan") as of June 1, 2020;
- 2,675,770 shares reserved to grant under the 2016 and 2019 Plans and an aggregate of 1,100,671 shares available for future grants under the 2019 Plan;
- 198,113 shares of our common stock issuable upon the exercise of warrants outstanding as of June 1, 2020; and
- 365,315 shares of our common stock reserved for future issuance under our 2019 Employee Stock Purchase Plan, or ESPP, as well as any future increases in the number of shares of common stock reserved for issuance under our ESPP.

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

The selling stockholders will receive all of the net proceeds from the sale of the shares of common stock offered hereby. We will not receive any proceeds from this offering.

SELLING STOCKHOLDERS

We have included in this prospectus and related registration statement 1,380,344 shares of our common stock issued in the Private Placement. 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; (iii) the maximum number of shares being offered by each selling stockholder pursuant to this prospectus; 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.

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 22,126,772 shares of common stock outstanding as of June 1, 2020, which includes the shares of our common stock registered for sale 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. 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.

None of the selling stockholders has, or within the past three years has had, any position, office or other material relationship with us or any of our affiliates. None of the selling stockholders is a broker-dealer or an affiliate of a broker-dealer, except as noted below.

Selling Stockholder ⁽¹⁾	Beneficial Ownership Before this Offering		Shares Offered Hereby	Beneficial Ownership After this Offering	
	Number of Shares Owned	Percentage of Outstanding Shares ⁽¹⁾		Number of Shares Owned ⁽²⁾	Percentage of Outstanding Shares ⁽¹⁾
OrbiMed Genesis Master Fund, LP	137,932	*	137,932	—	—
OrbiMed Partners Master Fund Limited	344,827	1.6%	344,827	—	—
The Biotech Growth Trust PLC	344,827	1.6%	344,827	—	—
Franklin Strategic Series — Franklin Biotechnology Discovery Fund	172,413	*	172,413	—	—
Franklin Templeton Investment Funds — Franklin Biotechnology Discovery Fund	172,413	*	172,413	—	—
Gregg Smith	37,503	*	6,897	30,606	*
Hessler Finance LTD	191,600	*	70,000	121,600	*
Timothy Hogue	43,571	*	13,793	29,778	*
Laurence Lytton	55,173	*	55,173	—	—
The Ryan and Brittany Pearson Living Trust	61,439	*	17,241	44,198	*
Reinfrank Living Trust	32,444	*	10,345	22,099	*
Richard A. Smith	180,393	*	34,483	145,910	*
Total:	<u>1,774,535</u>	<u>8.0%</u>	<u>1,380,344</u>	<u>394,191</u>	<u>1.8%</u>

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

(1) This table is based upon information supplied by the selling stockholders and is based on 22,126,772 shares of common stock outstanding as of June 1, 2020.

(2) Assumes sale of all of the shares of common stock offered hereby.

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 of 1933, as amended, 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

Certain legal matters related to the common stock offered in this prospectus will be passed upon for us by Skadden, Arps, Slate, Meagher & Flom LLP, New York, New York.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2019, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.



1,380,344 Shares of Common Stock

PRELIMINARY PROSPECTUS

, 2020

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, and the Nasdaq Global Market, or Nasdaq, listing fee.

SEC Registration Fee	\$ 3,618
FINRA Filing Fee	0
Nasdaq Listing Fee	0
Printing Expenses	75,000
Legal Fees and Expenses	50,000
Accounting Fees and Expenses	30,000
Transfer Agent Fees and Expenses	0
Miscellaneous	10,000
Total	<u>\$168,618*</u>

* Amounts previously paid in connection with the registration statement on Form S-1 declared effective on December 20, 2020.

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	Incorporated by Reference			
		Form	File No.	Exhibit	Filing Date
4.1	Registration Rights Agreement, dated November 7, 2019, by and among the Company and the Purchasers.	8-K	001-38898	10.2	November 12, 2019
4.2	Form of Common Stock Certificate	S-1/A	333-230838	4.1	April 24, 2019
4.3	Amended and Restated Investors' Rights Agreement, by and among the Registrant and certain of its stockholders, dated November 5, 2018	S-1/A	333-230838	4.2	April 29, 2019
4.4	Form of Warrant, issued to affiliates of Brookline Capital Markets, a division of CIM Securities LLC, on March 13, 2017.	S-1/A	333-230838	4.3	April 29, 2019
4.5	Form of Warrant, issued to affiliates of Brookline Capital Markets, a division of CIM Securities LLC, on November 5, 2018.	S-1/A	333-230838	4.4	April 29, 2019
4.6	Form of Warrant, issued to affiliates of Brookline Capital Markets, a division of CIM Securities LLC, on April 9, 2019.	S-1/A	333-230838	4.5	April 29, 2019
5.1	Opinion of Skadden, Arps, Slate, Meagher & Flom LLP.	S-1/A	333-235504	5.1	December 19, 2019

Exhibit No.	Description	Incorporated by Reference			
		Form	File No.	Exhibit	Filing Date
23.1	Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm.				
23.2	Consent of Skadden, Arps, Slate, Meagher & Flom LLP (included in Exhibit 5.1).	S-1/A	333-235504	5.1	December 19, 2019
24.1	Powers of Attorney.	S-1	333-235504	24.1	December 13, 2019

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.

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 appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

Consent of Independent Registered Public Accounting Firm

We consent to the reference to our firm under the caption "Experts" and to the use of our report dated March 13, 2020 in the Post Effective Amendment No. 2 to the Registration Statement (Form S-1 No. 333-235504) on Form S-3 and related Prospectus of Applied Therapeutics, Inc. for the registration of shares of its common stock.

/s/ Ernst & Young LLP

New York, New York
June 4, 2020
