

**Up to \$100,000,000 of Common Stock****Applied Therapeutics, Inc.**

We have entered into an equity distribution agreement with Cowen and Company, LLC, as our sales agent, under which we may offer and sell from time to time our common stock, par value \$0.0001 per share, or common stock, having an aggregate offering price of up to \$100,000,000. The sales agent may act as an agent on our behalf or purchase shares of our common stock as a principal. Under the terms of the equity distribution agreement, if we sell shares to the sales agent as a principal, we will enter into a separate terms agreement with the sales agent.

Our common stock is listed on The Nasdaq Global Market under the trading symbol "APLT". The last reported sales price of our common stock on The Nasdaq Global Market on January 25, 2022 was \$3.31 per share.

We are an "emerging growth company" as that term is used in the Jumpstart Our Business Startups Act of 2012 and, as such, have elected to comply with certain reduced public company reporting requirements for the prospectus supplement and future filings.

Sales of our common stock, if any, under this prospectus supplement and the accompanying prospectus, may be made in sales deemed to be "at the market offerings" as defined in Rule 415(a)(4) under the Securities Act of 1933, as amended, or the Securities Act, in ordinary brokers' transactions, to or through a market maker, on or through The Nasdaq Global Market or any other market venue where the securities may be traded, in the over-the-counter market, in privately negotiated transactions or through a combination of any such methods of sale. The sales agent may also sell our common stock by any other method permitted by law. The securities may be sold at market prices prevailing at the time of sale, at prices related to such prevailing market prices or at negotiated prices. The sales agent will make all sales using reasonable efforts consistent with its normal trading and sales practices, on mutually agreed terms between the sales agent and us. The sales agent is not required to sell any specific number or dollar amount of shares of our common stock, but subject to the terms and conditions of the equity distribution agreement, has agreed to use its reasonable efforts consistent with its normal trading and sales practices to sell shares of our common stock up to the amount specified. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

Pursuant to the terms of the equity distribution agreement, the sales agent will be entitled to compensation of up to 3% of the gross offering proceeds of all shares of our common stock sold through it as sales agent pursuant to the equity distribution agreement. We may also sell shares of our common stock directly to the sales agent, acting as principal, at prices agreed upon at the time of sale. In connection with the sale of shares of our common stock on our behalf, the sales agent may be deemed to be "underwriters" within the meaning of the Securities Act, and the compensation paid to the sales agent may be deemed to be underwriting commissions or discounts.

*Investing in our common stock involves a high degree of risk. Before making an investment decision, please read the information contained in and incorporated by reference under the heading "Risk Factors" on page S-4 of this prospectus supplement and on page 6 of the accompanying prospectus, and under similar headings in the other documents that we have filed or that are filed after the date hereof and incorporated by reference into this prospectus supplement and the accompanying prospectus.*

**Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.**

**COWEN**

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## ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and accompanying prospectus are part of a registration statement that we have filed with the Securities and Exchange Commission, or the SEC. Under this shelf registration statement, of which this prospectus supplement is a part, we may, from time to time, sell shares of our common stock having an aggregate gross sales price of up to \$100,000,000.

This document contains two parts. The first part is this prospectus supplement, which describes the specific terms of this offering and the securities offered hereby, and also adds to and updates information contained in the accompanying prospectus and the documents incorporated into each by reference. The second part, the accompanying prospectus, gives more general information about us, some of which may not apply to this offering. This prospectus supplement is deemed to be incorporated by reference into the accompanying prospectus solely for the purpose of this offering. When we refer only to the "prospectus," we are referring to both parts combined.

If there is any inconsistency between information in or incorporated by reference into the accompanying prospectus and information in or incorporated by reference into this prospectus supplement, the information contained in the most recently dated document shall control. This prospectus supplement, the accompanying prospectus and the documents incorporated into each by reference include important information about us, the common stock being offered and other information you should know before investing. You should read this prospectus supplement and the accompanying prospectus together with the additional information described under the heading "Where You Can Find More Information" before investing in our common stock.

For further information about us, you should refer to that registration statement, which you can obtain from the SEC as described elsewhere in this prospectus supplement under "Where You Can Find More Information."

Neither we nor the sales agent have authorized anyone to provide any information or to make any representations other than those contained in this prospectus supplement, the accompanying prospectus or in any free writing prospectuses prepared by or on behalf of us or to which we have referred you. No dealer, salesperson or other person is authorized to give any information or to represent anything not contained in this prospectus supplement and the accompanying prospectus. We and the sales agent take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus supplement is not an offer to sell or solicitation of an offer to buy these securities in any circumstances under which the offer or solicitation is unlawful. We are offering to sell, and seeking offers to buy, our securities offered hereby only in jurisdictions where offers and sales are permitted. You should not assume that the information we have included in this prospectus supplement or the accompanying prospectus is accurate as of any date other than the date of this prospectus supplement or the accompanying prospectus, respectively, or that any information we have incorporated by reference is accurate as of any date other than the date of the document incorporated by reference, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or of any of our securities. Our business, financial condition, results of operations and prospects may have changed since those dates.

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

## WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC under the Securities Exchange Act of 1934, or 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 supplement and the accompanying prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus supplement and the accompanying prospectus, except for any information superseded by information contained directly in this prospectus supplement and the accompanying prospectus, any subsequently filed document deemed incorporated by reference or any free writing prospectus prepared by or on behalf of us. This prospectus supplement incorporates

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, 2020, filed with the SEC on March 18, 2021;](#)
- the information specifically incorporated by reference into our [Annual Report on Form 10-K for the fiscal year ended December 31, 2020](#) from our [definitive proxy statement on Schedule 14A, filed with the SEC on April 21, 2021;](#)
- our Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2021, June 30, 2021 and September 30, 2021, filed with the SEC on [May 11, 2021](#), [August 12, 2021](#) and [November 12, 2021](#), respectively;
- our Current Reports on Form 8-K, filed with the SEC on [February 17, 2021](#) and [June 4, 2021](#); 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 after the date of this prospectus supplement and the accompanying 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 supplement and any documents incorporated by reference contain “forward-looking statements” within the meaning of Section 27A of the Securities Act, and Section 21E of 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 supplement and the accompanying prospectus 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 supplement and the accompanying prospectus 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, market and commercialize our product candidates;
- the initiation, timing, progress, results of, or any delays in, our current and future preclinical studies and clinical trials and our research and development programs;
- our ability to take advantage of expedited regulatory pathways for any of our product candidates;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our ability to successfully acquire or license additional product candidates on reasonable terms and advance product candidates into, and successfully complete, clinical studies;
- our ability to maintain and establish collaborations or obtain additional funding;
- our ability to obtain and timing of regulatory approval of our current and future product candidates;
- the anticipated indications for our product candidates, if approved;
- our expectations regarding the potential market size and the rate and degree of market acceptance of such product candidates;
- our ability to fund our working capital requirements and expectations regarding the sufficiency of our capital resources;
- the implementation of our business model and strategic plans for our business and product candidates;
- our intellectual property position and the duration of our patent rights;
- developments or disputes concerning our intellectual property or other proprietary rights;
- 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;
- our expected use of proceeds from this offering; and
- other factors that may impact our financial results.

The foregoing list of risks 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 supplement and the accompanying prospectus 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 sections titled "Risk Factors" in this prospectus supplement and the accompanying prospectus, 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 statements, whether as a result of new information, future events or otherwise.

## SUMMARY

*This summary highlights key aspects of this offering and certain information contained elsewhere in this prospectus supplement and the accompanying prospectus and the documents incorporated by reference. This summary is not complete and does not contain all of the information that may be important to you or that you should consider before investing in our common stock. You should read carefully the other information included and incorporated by reference in this prospectus supplement and the accompanying prospectus before investing in our common stock. You should pay special attention to the risks and uncertainties identified under the captions "Risk Factors," "Cautionary Note Regarding Forward-Looking Statements" and elsewhere in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein or therein, including our [Quarterly Report on Form 10-Q for the quarter ended September 30, 2021](#), when determining whether an investment in our common stock is appropriate for you. Unless the context otherwise requires, the terms "Applied Therapeutics," "the company," "we," "us," "our" and similar references in this prospectus refer to Applied Therapeutics, Inc.*

### Applied Therapeutics, Inc.

#### 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 can move quickly through the development process.

#### Recent Developments

##### *Cash Update*

As of December 31, 2021, we had approximately \$81 million of cash, cash equivalents and marketable securities. These amounts are unaudited and preliminary, and do not present all information necessary for an understanding of our financial condition as of December 31, 2021. The audit of our financial statements for the year ended December 31, 2021 is ongoing and could result in changes to these amounts. Our audited financial statements for the year ended December 31, 2021 will not be available until we file our annual report on Form 10-K for the year ended December 31, 2021.

Our expectations with respect to our unaudited results for the period discussed above are based upon management estimates and are the responsibility of management. Our independent registered public accounting firm has not audited, reviewed or performed any procedures with respect to these preliminary results and, accordingly, does not express an opinion or any other form of assurance about them.

##### *Regulatory Update on Galactosemia Program*

On January 3, 2022, we disclosed that we would hold on submitting our New Drug Application, or NDA, to the U.S. Food and Drug Administration, or FDA for AT-007 for treatment of Galactosemia pending

additional discussions with the FDA. Although the Galactosemia program had previously been discussed in the context of an NDA for Accelerated Approval based on reduction in galactitol, the FDA indicated at the end of 2021 that clinical outcomes data will likely be required for approval. We are in active discussion and collaboration with the FDA regarding a path forward for the Galactosemia NDA submission.

*Initiation of Registrational Phase 2/3 Study of AT-007 in SORD Deficiency*

On December 16, 2021, we announced the initiation of a registrational phase 2/3 study of AT-007 in Sorbitol Dehydrogenase Deficiency, or SORD. The study, termed INSPIRE (Inhibition of Sorbitol Production through Inhibition of the Aldose Reductase Enzyme), is investigating biomarker efficacy, clinical outcomes and safety in people living with SORD deficiency treated with AT-007 compared to a placebo.

**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.



**THE OFFERING**

*The following summary contains basic information about the offering and is not intended to be complete. It does not contain all the information that is important to you. You should carefully read the entire prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein before making an investment decision.*

<b>Issuer</b>	Applied Therapeutics, Inc., a Delaware Corporation.
<b>Securities</b>	Common stock having an aggregate offering price of up to \$100,000,000.
<b>Manner of offering</b>	From time to time by us through or to the sales agent, acting as an agent on our behalf or a principal, including “at-the-market” offerings, as applicable. See “Plan of Distribution.”
<b>Use of proceeds</b>	We intend to use the net proceeds for general corporate purposes. See “Use of Proceeds” on page S-7 of this prospectus supplement.
<b>Risk factors</b>	This investment involves a high degree of risk. See “Risk Factors” beginning on page S-4 of this prospectus supplement, page 6 of the accompanying prospectus and in the documents incorporated by reference herein (including under “Risk Factors” in our most recent Annual Report on Form 10-K or Quarterly Report on Form 10-Q, as applicable) for a discussion of the risks you should carefully consider before deciding to invest in our common stock.
<b>Nasdaq Global Market Symbol</b>	“APLT”

## RISK FACTORS

*Investing in our common stock is speculative and involves a high degree of risk. The following risk factors, as well as risks currently unknown to us, could materially adversely affect our future business, operations and financial condition and could cause them to differ materially from the estimates described in forward-looking information relating to us, or our business, property or financial results, each of which could cause purchasers of our common stock to lose part or all of their investment. In addition to the other information contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein, prospective investors should carefully consider the factors set out under "Risk Factors" in the accompanying prospectus and our most recent Annual Report on Form 10-K or Quarterly Report on Form 10-Q, as applicable, and the factors set out below before deciding to invest in our common stock.*

### **Risks Related to This Offering and Ownership of Our Common Stock**

***The market price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock.***

The market price of our common stock is likely to be volatile. The stock market in general and the market for biopharmaceutical and pharmaceutical companies in particular, has experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your common stock at or above the price paid for the shares in this offering. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this prospectus supplement and the accompanying prospectus, the market price for our common stock may be influenced by the following:

- 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;
- the commencement, enrollment, results of, or any delays in our planned or future clinical trials of our product candidates or those of our competitors;
- the success of competitive drugs or therapies;
- regulatory or legal developments in the United States and other countries;
- the success of competitive products or technologies;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to our product candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- our inability to obtain or delays in obtaining adequate drug supply for any approved drug or inability to do so at acceptable prices;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- significant lawsuits, including patent or stockholder litigation;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems, including coverage and adequate reimbursement for any approved drug;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, political, and market conditions and overall fluctuations in the financial markets in the United States and abroad; and
- investors' general perception of us and our business.

These and other market and industry factors may cause the market price and demand for our common stock to fluctuate substantially, regardless of our actual operating performance, which may

limit or prevent investors from selling their shares at or above the price paid for their shares in this offering and may otherwise negatively affect the liquidity of our common stock. Furthermore, we believe our stock has been, and may in the future be, adversely affected as a result of actions taken by third-parties. Short sellers and others, some of whom post anonymously on social media, may be positioned to profit if our stock declines and their activities can negatively affect our stock price.

Some companies that have experienced volatility in the trading price of their shares have been the subject of securities class action litigation. Any lawsuit to which we are a party, with or without merit, may result in an unfavorable judgment. We also may decide to settle lawsuits on unfavorable terms. Any such negative outcome could result in payments of substantial damages or fines, damage to our reputation or adverse changes to our business practices.

Defending against litigation is costly and time-consuming, and could divert our management's attention and our resources. Furthermore, during the course of litigation, there could be negative public announcements of the results of hearings, motions or other interim proceedings or developments, which could have a negative effect on the market price of our common stock.

***Concentration of ownership of our common stock among our existing executive officers, directors and principal stockholders may prevent new investors from influencing significant corporate decisions.***

Based upon shares of our common stock outstanding as of December 31, 2021, our executive officers, directors and stockholders who owned more than 5% of our outstanding common stock, in the aggregate, beneficially own shares representing approximately 35.7% of our outstanding common stock. If our executive officers, directors and stockholders who owned more than 5% of our outstanding common stock acted together, they may be able to significantly influence all matters requiring stockholder approval, including the election and removal of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. The concentration of voting power and transfer restrictions could delay or prevent an acquisition of our company on terms that other stockholders may desire or result in the management of our company in ways with which other stockholders disagree.

***If research analysts do not publish research or reports, or publish unfavorable research or reports, about us, our business or our market, our stock price and trading volume could decline.***

The trading market for our common stock will be influenced by the research and reports that industry or financial analysts publish about us or our business. Equity research analysts may discontinue research coverage of our common stock, and such lack of research coverage may adversely affect the market price of our common stock. We do not have any control over the analysts or the content and opinions included in their reports. The price of our shares could decline if one or more equity research analysts downgrade our shares or issue other unfavorable commentary or research about us. If one or more equity research analysts cease coverage of us or fail to publish reports on us regularly, demand for our shares could decrease, which in turn could cause the trading price or trading volume of our common stock to decline.

***If you purchase shares of common stock in this offering, you will suffer immediate dilution of your investment.***

We cannot predict the effect, if any, that future sales of our common stock, including sales pursuant to the equity distribution agreement, or the availability of our common stock for future sale, will have on the market price of our common stock. Future sales or issuances of our common stock may dilute the ownership interests of our existing stockholders, including purchasers of common stock in this offering. In addition, we also have outstanding options and warrants to purchase common stock with exercise prices lower than the price we expect investors in this offering to pay for shares of common stock. To the extent these outstanding options or warrants are exercised, there will be further dilution to investors. The perception that such sales or issuances may occur could also negatively impact the market price of our common stock.

***Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain.***

You should not rely on an investment in our common stock to provide dividend income. We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our

future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future. Investors seeking cash dividends should not purchase our common stock.

***We have broad discretion in the use of our cash and cash equivalents, including the net proceeds from this offering, and may use them ineffectively, in ways with which you do not agree or in ways that do not increase the value of your investment.***

Our management has broad discretion in the application of our cash and cash equivalents, including the net proceeds from this offering, and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in additional operating losses that could have a negative impact on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest our cash and cash equivalents, including the net proceeds from this offering, in a manner that does not produce income or that loses value. See “Use of Proceeds” for additional information.

***Future sales of common stock by holders of our common stock, or the perception that such sales may occur, could depress the market price of our common stock.***

Sales of a substantial number of shares of our common stock in the public market could occur at any time, subject to certain restrictions described below. These sales, or the perception in the market that holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. As of December 31, 2021, we had outstanding 26,215,514 shares of common stock. A substantial number of such shares are currently restricted as a result of securities laws but will be able to be sold in the future.

We further have registered all shares of common stock that we may issue in the future or have issued to date under our equity compensation plans. These shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates. Sales of a large number of the shares issued under these plans in the public market could have an adverse effect on the market price of our common stock.

## USE OF PROCEEDS

We intend to use the net proceeds from this offering 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.

Pending such use of the net proceeds from this offering, we intend to hold some amounts as cash and to invest the remaining net proceeds in a variety of capital preservation investments, including short-term investment-grade, interest-bearing instruments denominated in currencies.

The expected use of the net proceeds from this offering represents our intentions based on our current plans and business conditions, which could change in the future as our plans and business conditions evolve. Further, due to the uncertainties inherent in the drug development process, it is difficult to estimate with certainty the exact amounts of the net proceeds from this offering that may be used for the above purposes.

## PLAN OF DISTRIBUTION

We have entered into an equity distribution agreement with Cowen and Company, LLC, as our sales agent, under which we may offer and sell from time to time our common stock having an aggregate offering price of up to \$100,000,000. The sales agent may act as an agent on our behalf or purchase shares of our common stock as a principal. Under the terms of the equity distribution agreement, if we sell shares to the sales agent as a principal, we will enter into a separate terms agreement with the sales agent. The equity distribution agreement will be filed under the Exchange Act as Exhibit 1.1 to our Current Report on Form 8-K, dated as of the date hereof, and will be incorporated by reference into this prospectus supplement.

Sales, if any, of common stock under the equity distribution agreement may be made in ordinary brokers' transactions, to or through a market maker, on or through The Nasdaq Global Market or any other market venue where the securities may be traded, in the over-the-counter market, in privately negotiated transactions or through a combination of any such methods of sale. The sales agent may also sell our common stock by any other method permitted by law.

The securities may be sold at market prices prevailing at the time of sale, at prices related to such prevailing market prices or at negotiated prices.

We will designate the maximum amount of common stock to be sold through the sales agent on a daily basis or otherwise as we and the sales agent agree and the minimum price per share at which such common stock may be sold. Subject to the terms and conditions of the equity distribution agreement, the sales agent will use its reasonable efforts consistent with its normal sales and trading practices to sell on our behalf all of the designated shares of common stock. We may instruct the sales agent not to sell any common stock if the sales cannot be effected at or above the price designated by us in any such instruction. We or the sales agent may suspend the offering of our common stock at any time and from time to time by notifying the other party in writing.

If shares of our common stock are sold by the sales agent in an at-the-market offering, the sales agent will provide to us written confirmation following the close of trading on The Nasdaq Global Market each trading day on which shares of our common stock are sold under the equity distribution agreement. Each confirmation will include the number of shares of our common stock sold on such day, the gross offering proceeds received from such sale and the compensation or commission payable by us to the sales agent with respect to such sales. We will report at least quarterly the number of shares of our common stock sold through the sales agent under the equity distribution agreement, the net proceeds to us (before expenses) and the compensation paid by us to the sales agent in connection with the sales of the shares of our common stock.

We will pay the sales agent a commission of up to 3% of the gross sales price per share of common stock sold through the sales agent under the equity distribution agreement. We have also agreed to reimburse the sales agent for certain of its expenses. We estimate that the total expenses of the offering payable by us, excluding discounts, commissions and reimbursements payable to the sales agent under the equity distribution agreement, will be approximately \$250,000.

Settlement of any sales of common stock will occur on the second trading day following the date on which such sales were made (or such earlier day as is industry practice for regular-way trading). There is no arrangement for funds to be received in an escrow, trust or similar arrangement. Sales of our common stock as contemplated in this prospectus supplement will be settled through the facilities of The Depository Trust Company or by such other means as we and the sales agent may agree.

The offering of our common stock pursuant to the equity distribution agreement will terminate upon the earlier of (i) the sale of all of our shares of common stock subject to the equity distribution agreement (ii) termination of the equity distribution agreement by us or by the sales agent as provided therein or (iii) the third anniversary of the date of the equity distribution agreement.

In connection with the sale of the shares of common stock on our behalf, the sales agent may be deemed to be an "underwriter" within the meaning of the Securities Act, and the compensation paid to each of the sales agent may be deemed to be underwriting commissions or discounts.

We have agreed to provide indemnification and contribution to the sales agent against certain liabilities, including civil liabilities under the Securities Act.

The sales agent is a full service financial institution engaged in various activities, which may include securities trading, investment banking, financial advisory, investment management, principal investment, hedging, financing and brokerage activities. The sales agent and its respective affiliates have in the past performed investment banking and advisory services for us from time to time for which it has received customary fees and reimbursement of expenses and may, from time to time, engage in transactions with and perform services for us in the ordinary course of its business for which it may receive customary fees and reimbursement of expenses. In the ordinary course of its various business activities, the sales agent and its respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (which may include bank loans and/or credit default swaps) for its own account and for the accounts of its customers and may at any time hold long and short positions in such securities and instruments. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The sales agent and its affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

### **Selling Restrictions**

#### *European Economic Area*

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

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

provided that no such offer of shares of common stock shall require the company or any sales agent to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation.

Each person in a Relevant State who initially acquires any shares of common stock or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with the company and the sales agent that it is a qualified investor within the meaning of the Prospectus Regulation.

In the case of any shares of common stock being offered to a financial intermediary as that term is used in Article 5(1) of the Prospectus Regulation, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares of common stock acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer to the public other than their offer or resale in a Relevant State to qualified investors, in circumstances in which the prior consent of the sales agent has been obtained to each such proposed offer or resale.

The Company, the sales agent and its affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

For the purposes of this provision, the expression an "offer to the public" in relation to any shares of common stock in any Relevant State means the communication in any form and by any means of

sufficient information on the terms of the offer and any shares to be offered so as to enable an investor to decide to purchase or subscribe for any shares, and the expression “Prospectus Regulation” means Regulation (EU) 2017/1129.

*United Kingdom*

In relation to the United Kingdom, or the UK, no shares of our common stock have been offered or will be offered pursuant to the offering to the public in the UK prior to the publication of a prospectus in relation to the shares of common stock which has been approved by the Financial Conduct Authority in the UK in accordance with the UK Prospectus Regulation and the FSMA, except that offers of shares of common stock may be made to the public in the UK at any time under the following exemptions under the UK Prospectus Regulation and the FSMA:

- (a) to any legal entity which is a qualified investor as defined under the UK Prospectus Regulation;
- (b) to fewer than 150 natural or legal persons (other than qualified investors as defined under the UK Prospectus Regulation), subject to obtaining the prior consent of the sales agent for any such offer; or
- (c) at any time in other circumstances falling within section 86 of the FSMA,

provided that no such offer of shares of common stock shall require the company or any sales agent to publish a prospectus pursuant to Section 85 of the FSMA or Article 3 of the UK Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the UK Prospectus Regulation.

Each person in the UK who initially acquires any shares of common stock or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with the company and the sale agent that it is a qualified investor within the meaning of the UK Prospectus Regulation.

In the case of any shares of common stock being offered to a financial intermediary as that term is used in Article 5(1) of the UK Prospectus Regulation, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer to the public other than their offer or resale in the UK to qualified investors, in circumstances in which the prior consent of the sales agent has been obtained to each such proposed offer or resale.

The company, the sales agent and its affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

For the purposes of this provision, the expression an “offer to the public” in relation to any shares of our common stock in the UK means the communication in any form and by any means of sufficient information on the terms of the offer and any shares of our common stock to be offered so as to enable an investor to decide to purchase or subscribe for any shares of our common stock, the expression “UK Prospectus Regulation” means Regulation (EU) 2017/1129 as it forms part of domestic law by virtue of the European Union (Withdrawal) Act 2018, and the expression “FSMA” means the Financial Services and Markets Act 2000.

This document is for distribution only to persons who (i) have professional experience in matters relating to investments and who qualify as investment professionals within the meaning of Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (as amended, the “Financial Promotion Order”), (ii) are persons falling within Article 49(2)(a) to (d) (“high net worth companies, unincorporated associations etc.”) of the Financial Promotion Order, (iii) are outside the United Kingdom, or (iv) are persons to whom an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the FSMA) in connection with the issue or sale of any securities may otherwise lawfully be communicated or caused to be communicated (all such persons together being referred to as “relevant persons”). This document is directed only at relevant persons and must not be acted on or relied on by persons who are not relevant persons. Any investment or investment activity to which this document relates is available only to relevant persons and will be engaged in only with relevant persons.



*Canada*

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

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

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

*Hong Kong*

The shares of common stock may not be offered or sold in Hong Kong by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32 of the Laws of Hong Kong) ("Companies (Winding Up and Miscellaneous Provisions) Ordinance") or which do not constitute an invitation to the public within the meaning of the Securities and Futures Ordinance (Cap. 571 of the Laws of Hong Kong) ("Securities and Futures Ordinance"), or (ii) to "professional investors" as defined in the Securities and Futures Ordinance and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a "prospectus" as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance, and no advertisement, invitation or document relating to the common stock may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to shares of common stock which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" in Hong Kong as defined in the Securities and Futures Ordinance and any rules made thereunder.

*Singapore*

This prospectus supplement has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares of common stock may not be circulated or distributed, nor may the shares of common stock be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor (as defined under Section 4A of the Securities and Futures Act, Chapter 289 of Singapore (the "SFA")) under Section 274 of the SFA, (ii) to a relevant person (as defined in Section 275(2) of the SFA) pursuant to Section 275(1) of the SFA, or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA, in each case subject to conditions set forth in the SFA.

Where the shares of common stock are subscribed or purchased under Section 275 of the SFA by a relevant person which is a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor, the securities (as defined in Section 239(1) of the SFA) of that corporation shall not be transferable for six months after that corporation has acquired the common stock under Section 275 of the SFA except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (2) where such transfer arises from an offer in that corporation's securities pursuant to Section 275(1A) of the SFA, (3) where no consideration is or will be given for the transfer, (4) where the

transfer is by operation of law, (5) as specified in Section 276(7) of the SFA, or (6) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore ("Regulation 32").

Where the shares of common stock are subscribed or purchased under Section 275 of the SFA by a relevant person which is a trust (where the trustee is not an accredited investor (as defined in Section 4A of the SFA)) whose sole purpose is to hold investments and each beneficiary of the trust is an accredited investor, the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferable for six months after that trust has acquired the shares of common stock under Section 275 of the SFA except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (2) where such transfer arises from an offer that is made on terms that such rights or interest are acquired at a consideration of not less than S\$200,000 (or its equivalent in a foreign currency) for each transaction (whether such amount is to be paid for in cash or by exchange of securities or other assets), (3) where no consideration is or will be given for the transfer, (4) where the transfer is by operation of law, (5) as specified in Section 276(7) of the SFA, or (6) as specified in Regulation 32.

#### *Japan*

The shares of common stock have not been and will not be registered under the Financial Instruments and Exchange Act of Japan (Act No. 25 of 1948, as amended), or the FIEA. The common stock may not be offered or sold, directly or indirectly, in Japan or to or for the benefit of any resident of Japan (including any person resident in Japan or any corporation or other entity organized under the laws of Japan) or to others for reoffering or resale, directly or indirectly, in Japan or to or for the benefit of any resident of Japan, except pursuant to an exemption from the registration requirements of the FIEA and otherwise in compliance with any relevant laws and regulations of Japan.

**LEGAL MATTERS**

Certain legal matters will be passed upon for us by Skadden, Arps, Slate, Meagher & Flom LLP, New York, New York. Certain legal matters in connection with this offering will be passed upon for the sales agent by Davis Polk & Wardwell 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, 2020](#), as set forth in their report, which is incorporated by reference in this prospectus supplement and the accompanying prospectus. 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.

PROSPECTUS

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## Applied Therapeutics, Inc.



**Common Stock  
Preferred Stock  
Depository Shares  
Debt Securities  
and  
Warrants**

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

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

We will provide the specific prices and terms of these securities in one or more supplements to this prospectus at the time of offering. You should read this prospectus and the accompanying prospectus supplement carefully before you make your investment decision.

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**This prospectus may not be used to sell securities unless accompanied by a prospectus supplement.**

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*Investing in our securities involves a number of risks. See "Risk Factors" on page 6 before you make your investment decision.*

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

Our common stock is listed on The Nasdaq Global Market under the trading symbol "APLT." On June 11, 2020, the last reported price of our common stock was \$39.96 per share. Each prospectus supplement will indicate whether the securities offered thereby will be listed on any securities exchange.

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

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**The date of this prospectus is June 15, 2020**

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## ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission (the “SEC”), using a “shelf” registration process. Under this process, we may sell from time to time any combination of the securities described in this prospectus. This prospectus only provides you with a general description of the securities that we may offer. Each time we sell securities, we will provide a supplement to this prospectus that contains specific information about the terms of that offering, including the specific amounts, prices and terms of the securities offered. The prospectus supplement may also add, update or change information contained in this prospectus. You should carefully read both this prospectus, any accompanying prospectus supplement and any free writing prospectus prepared by or on behalf of us, together with the additional information described under the heading “Where You Can Find More Information.”

We have not 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 take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We are not making offers to sell the securities in any jurisdiction in which an offer or solicitation is not authorized or in which the person making such offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make an offer or solicitation.

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

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

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

## WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC under the Securities Exchange Act of 1934, as amended (the “Exchange Act”). Our SEC filings are available to the public at the SEC’s website at [www.sec.gov](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, 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 \(only with respect to Item 8.01\)](#), [May 26, 2020](#) and [June 5, 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 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.



## 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.

## 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.

### 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

Except as otherwise set forth in any accompanying prospectus supplement, we expect to use the net proceeds from the sale of securities 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.

## DESCRIPTION OF SECURITIES

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

## DESCRIPTION OF CAPITAL STOCK

### General

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

Our authorized capital stock consists of 100,000,000 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 June 1, 2020, 22,126,772 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**

Certain holders of shares of our common stock, including those shares of our common stock that were issued upon the conversion of our preferred stock in connection with our initial public offering in May 2019 ("IPO"), are entitled to certain rights with respect to registration of such shares 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 amended and restated investors' rights agreement, by and among us and certain of our stockholders, dated as of November 5, 2018 (the "Investors' Rights Agreement"). The registration of shares of our common stock 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 demand, piggyback and Form S-3 registrations described in the Investors' Rights Agreement.

Generally, in an underwritten offering, the managing underwriter, if any, has the right, subject to specified conditions and limitations, to limit the number of shares the holders may include. The demand, piggyback and Form S-3 registration rights described in the Investors' Rights Agreement will expire no later than three years after the completion of the IPO, or with respect to any particular holder, at such time that such holder can sell its shares under Rule 144 of the Securities Act during any three-month period.

### **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<sup>2</sup>/<sub>3</sub>% 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 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.

#### **LISTING**

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

#### **TRANSFER AGENT AND REGISTRAR**

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



## DESCRIPTION OF DEPOSITARY SHARES

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

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

### Dividends and Other Distributions

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

### Redemption of Depositary Shares

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

### Voting the Preferred Stock

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

### Amendment and Termination of the Depositary Agreement

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

## DESCRIPTION OF DEBT SECURITIES

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

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

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

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

- provisions granting special rights to holders of the debt securities upon occurrence of specified events;
- additions or changes relating to compensation or reimbursement of the trustee of the series of debt securities;
- provisions relating to the modification of the indenture both with and without the consent of holders of debt securities issued under the indenture and the execution of supplemental indentures for such series; and
- any other terms of the debt securities (which terms shall not be inconsistent with the provisions of the TIA, but may modify, amend, supplement or delete any of the terms of the indenture with respect to such series of debt securities).

### **General**

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

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

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

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

### **Global Securities**

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

### **Governing Law**

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

## DESCRIPTION OF WARRANTS

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

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

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

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

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

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

## PLAN OF DISTRIBUTION

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

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

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

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

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

### **Sale through Underwriters or Dealers**

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

During and after an offering through underwriters, the underwriters may purchase and sell the securities in the open market. These transactions may include overallotment and stabilizing transactions and purchases to cover syndicate short positions created in connection with the offering. The underwriters may also impose a penalty bid, which means that selling concessions allowed to syndicate members or other broker-dealers for the offered securities sold for their account may be reclaimed by

the syndicate if the offered securities are repurchased by the syndicate in stabilizing or covering transactions. These activities may stabilize, maintain or otherwise affect the market price of the offered securities, which may be higher than the price that might otherwise prevail in the open market. If commenced, the underwriters may discontinue these activities at any time.

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

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

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

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

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

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

#### **Direct Sales and Sales through Agents**

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

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

#### **At the Market Offerings**

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

#### **Remarketing Arrangements**

Securities may also be offered and sold, if so indicated in the applicable prospectus supplement, in connection with a remarketing upon their purchase, in accordance with a redemption or repayment

pursuant to their terms, or otherwise, by one or more remarketing firms, acting as principals for their own accounts or as agents for us. Any remarketing firm will be identified and the terms of its agreements, if any, with us and its compensation will be described in the applicable prospectus supplement.

#### **Delayed Delivery Contracts**

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

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

#### **General Information**

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

### **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, 2019](#), 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 incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.



Up to \$100,000,000 of

Common Stock

**Applied Therapeutics, Inc.**

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PROSPECTUS SUPPLEMENT

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**Cowen**

January 26, 2022

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