

Subject to completion, dated June 22, 2022

**Preliminary Prospectus Supplement
(To Prospectus dated June 15, 2020)****Shares
Pre-Funded Warrants to Purchase up to
Warrants to Purchase up to
Shares****Common Stock**

We are offering _____ shares of our common stock, par value \$0.0001 per share, and accompanying warrants to purchase up to _____ shares of our common stock (the common warrants) (and the shares of common stock issuable from time to time upon exercise of such common warrants) pursuant to this prospectus supplement and the accompanying prospectus. Each share of common stock sold in this offering will be accompanied by a common warrant to purchase one share of our common stock at an exercise price of \$ _____ per share. The shares of common stock and common warrants can only be purchased together in this offering but will be issued separately and will be immediately separable upon issuance. Subject to certain ownership limitations, the common warrants will be exercisable immediately, and the common warrants will expire on the _____ anniversary of the date of issuance.

We are also offering, for certain investors that so choose, pre-funded warrants to purchase an aggregate of _____ shares of common stock (the pre-funded warrants) (and the shares of common stock issuable from time to time upon exercise of the pre-funded warrants), in lieu of shares of common stock, and accompanying common warrants to purchase _____ shares of our common stock. Each pre-funded warrant will be exercisable for one share of common stock at an exercise price of \$ _____ per share of common stock. The public offering price is \$ _____ per pre-funded warrant and accompanying common warrant, which is equal to the public offering price per share of common stock and accompanying common warrant less \$ _____. Each pre-funded warrant will be exercisable upon issuance and will expire on the _____ anniversary of the date of issuance. The shares of common stock or pre-funded warrants, as applicable, and the accompanying common warrants, can only be purchased together in this offering but will be issued separately and will be immediately separable upon issuance. We refer to the shares of common stock issued in this offering, the pre-funded warrants and the common warrants, collectively, as the securities.

Our common stock is listed on The Nasdaq Global Market, or Nasdaq, under the trading symbol "APLT." The last reported sales price of our common stock on The Nasdaq Global Market on June 17, 2022 was \$1.05 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 this prospectus supplement and future filings.

There is no established public trading market for the pre-funded warrants or the common warrants, and we do not expect a market to develop. In addition, we do not intend to list the pre-funded warrants or the common warrants, nor do we expect the pre-funded warrants or the common warrants to be quoted, on Nasdaq or any other national securities exchange or any other nationally recognized trading system. Without an active trading market, the liquidity of the pre-funded warrants and the common warrants will be limited.

Investing in our securities 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-8 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.

	Per Share and Accompanying Common Warrant	Per Pre-Funded Warrant and Accompanying Common Warrant	Total
Public offering price	\$	\$	\$
Underwriting discounts and commissions ⁽¹⁾	\$	\$	\$
Proceeds, before expenses, to us	\$	\$	\$

(1) We have agreed to reimburse the underwriter for certain FINRA-related expenses. See "Underwriting" for a description of the compensation payable to the underwriter.

Entities affiliated with Alexandria Venture Investments, LLC ("Alexandria Venture"), which, as of March 31, 2022, owned 13.1% of our outstanding common stock, have indicated to us that they may choose to purchase additional shares of common stock and common warrants, or pre-funded warrants and common warrants, in this offering. The amount of such investment could be a significant portion of the securities sold in this offering. However, because indications of interest are not binding agreements or commitments to purchase, Alexandria Venture may determine to purchase fewer securities or not to purchase any securities in this offering. In addition, the underwriter could determine to sell fewer securities to Alexandria Venture than Alexandria Venture has an interest in purchasing or not to sell any securities to Alexandria Venture. The underwriter will receive the same underwriting discount on any securities purchased by Alexandria Venture as it will on any other securities sold to the public in this offering. Any securities sold to Alexandria Venture will be subject to the lock-up agreements described under "Underwriting."

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.

The underwriter expects to deliver the securities to purchasers on or about June _____, 2022.

Sole Book-Running Manager

SVB Securities

Prospectus supplement dated June _____, 2022

The information in this preliminary prospectus supplement is not complete and may be changed. Neither this preliminary prospectus supplement nor the accompanying prospectus is an offer to sell these securities nor does it solicit offers to buy these securities in any jurisdiction where such offer or sale is not permitted.

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Prospectus

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ABOUT THIS PROSPECTUS SUPPLEMENT

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 securities 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 securities.

Neither we nor the underwriter 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. We and the underwriter 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.

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, 2021, filed with the SEC on March 10, 2022;](#)
- the information specifically incorporated by reference into our [Annual Report on Form 10-K for the fiscal year ended December 31, 2021](#) from our [definitive proxy statement on Schedule 14A, filed with the SEC on April 15, 2022;](#)
- [our Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2022, filed with the SEC on May 12, 2022;](#)
- our Current Reports on Form 8-K, filed with the SEC on [January 26, 2022](#), [January 28, 2022](#) and [June 3, 2022](#); 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 of 1933, as amended, or 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:

- our plans to develop, market and commercialize our product candidates;
- the initiation, timing, progress and results of our current and future preclinical studies and clinical trials and our research and development programs;
- our ability to take advantage of expedited regulatory pathways for any of our product candidates;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our ability to successfully acquire or license additional product candidates on reasonable terms and advance product candidates into, and successfully complete, clinical studies;
- our ability to maintain and establish collaborations or obtain additional funding;
- our ability to obtain and timing of regulatory approval of our current and future product candidates;
- the anticipated indications for our product candidates, if approved;
- our expectations regarding the potential market size and the rate and degree of market acceptance of such product candidates;
- our ability to fund our working capital requirements and expectations regarding the sufficiency of our capital resources;
- the implementation of our business model and strategic plans for our business and product candidates;
- our intellectual property position and the duration of our patent rights;
- developments or disputes concerning our intellectual property or other proprietary rights;
- the potential impact of the Covid-19 pandemic on the timing and progress of our ongoing clinical trials, our business, results of operations, liquidity, and operations and our ability to mitigate those potential impacts;
- our expectations regarding government and third-party payor coverage and reimbursement;
- our ability to compete in the markets we serve;
- the impact of government laws and regulations and liabilities thereunder;
- developments relating to our competitors and our industry;
- 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. Other sections of this prospectus supplement may include additional factors that could harm our business and financial performance. 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 a 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 securities. You should read carefully the other information included and incorporated by reference in this prospectus supplement and the accompanying prospectus before investing in our securities. 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 March 31, 2022](#), when determining whether an investment in our securities 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.

Overview

We are a clinical-stage biopharmaceutical company developing a pipeline of novel product candidates against validated molecular targets in indications of high unmet medical need. We focus on molecules and pathways whose role in the disease process is well known based on prior research, but have previously failed to yield successful products due to poor efficacy and tolerability. Our unique approach to drug development leverages recent technological advances to design improved drugs, employs early use of biomarkers to confirm biological activity and focuses on abbreviated regulatory pathways. Our first molecular target is aldose reductase, or AR, an enzyme that converts glucose to sorbitol under oxidative stress conditions, and is implicated in multiple diseases. Prior attempts to inhibit this enzyme were hindered by nonselective, nonspecific inhibition, which resulted in limited efficacy and significant off-target safety effects. The detrimental consequences of AR activation have been well established by decades of prior research. Our AR program currently includes three small molecules, which are all potent and selective inhibitors of AR, but are engineered to have unique tissue permeability profiles to target different disease states, including diabetic complications, heart disease and rare metabolic diseases. Using similar strategies to our ARI program, we have also developed a program targeting selective inhibition of phosphatidylinositol 3-kinase, or PI3K, subunits, which has 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.

Recent Developments

On June 3, 2022, we announced that one of our product candidates, AT-007, received orphan medicinal product designation by the European Medicines Agency (“EMA”) for treatment of Galactosemia (Galactosaemia). We plan to meet with the EMA to discuss a potential marketing authorization application submission in Europe for conditional approval based on available biomarker data or for full approval based on expected clinical outcomes data.

Our Corporate Information

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

THE OFFERING**Common stock offered by us**

shares of common stock.

Pre-funded warrants offered by us

We are offering pre-funded warrants to purchase an aggregate of _____ shares of our common stock. We are offering to each purchaser the opportunity to purchase, if the purchaser so chooses, pre-funded warrants, in lieu of shares of common stock. Each pre-funded warrant will be exercisable for one share of our common stock. The purchase price of each pre-funded warrant will equal the price per share at which the shares of common stock are being sold to the public in this offering minus \$ _____, and the exercise price of each pre-funded warrant will be \$ _____ per share. This prospectus supplement also relates to the shares of common stock issuable upon exercise of any pre-funded warrants sold in this offering. The exercise price and number of shares of common stock issuable upon exercise will be subject to certain further adjustments as described herein. There is no established public trading market for the pre-funded warrants being offered in this offering, and we do not expect a market to develop. In addition, we do not intend to apply for a listing of the pre-funded warrants on any securities exchange. Without an active market, the liquidity of the pre-funded warrants will be limited. See "Description of Warrants" below.

Common warrants offered by us

We are offering common warrants to purchase an aggregate of _____ shares of our common stock. Each share of our common stock and each pre-funded warrant to purchase one share of our common stock is being sold together with one common warrant to purchase one share of our common stock. Each common warrant has an exercise price of \$ _____ per share, is immediately exercisable and will expire on the _____ year anniversary of the date of issuance. This prospectus supplement also relates to the offering of the shares of common stock issuable upon exercise of the common warrants. The exercise price and number of shares of common stock issuable upon exercise will be subject to certain further adjustments as described herein. There is no established public trading market for the common warrants being offered in this offering, and we do not expect a market to develop. In addition, we do not intend to apply for a listing of the common warrants on any securities exchange. Without an active market, the liquidity of the common warrants will be limited. For additional information regarding the common warrants, see "Description of Warrants" below.

Common stock to be outstanding immediately after this offering

_____ shares of common stock, assuming all of the pre-funded warrants issued in this offering are exercised and no exercise of any common warrants issued in this offering.

Use of proceeds

We estimate that our net proceeds from this offering will be approximately \$ _____ million, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

	We intend to use the net proceeds from this offering for general corporate purposes. See “Use of Proceeds” for additional information.
Risk factors	See “Risk Factors” beginning on page S-8 of this prospectus supplement and other information included and incorporated by reference in this prospectus supplement and the accompanying prospectus for a discussion of factors that you should carefully consider before deciding to invest in our securities.
Market symbol	Our common stock currently is listed on Nasdaq under the symbol “APLT.” There is no established public trading market for the pre-funded warrants or the common warrants, and we do not expect a market to develop. In addition, we do not intend to list the pre-funded warrants or the common warrants, nor do we expect the pre-funded warrants or the common warrants to be quoted, on Nasdaq or any other national securities exchange or any other nationally recognized trading system. Without an active trading market, the liquidity of the pre-funded warrants and the common warrants will be limited.
	The number of shares of our common stock to be outstanding after this offering set forth above is based on 26,215,514 shares of our common stock outstanding as of March 31, 2022 and excludes:
	<ul style="list-style-type: none"> • options to purchase 4,851,565 shares of common stock outstanding under the 2016 Plan and the 2019 Plan; • restricted stock units to purchase 551,468 shares of common stock outstanding under the 2019 Plan; • 2,823,766 shares reserved to grant under the 2016 and 2019 Plans and 1,379,543 shares available for future grants under the 2019 Plan; • 125,618 shares of our common stock issuable upon the exercise of warrants outstanding; • 487,092 shares of our common stock reserved for future issuance under our 2019 Employee Stock Purchase Plan, or ESPP, as well as any future increases in the number of shares of common stock reserved for issuance under our ESPP; and • shares of common stock issuable upon exercise of the pre-funded warrants and common warrants issued in this offering.
	Unless otherwise indicated, all information in this prospectus supplement assumes no exercise of the outstanding options and warrants described above after March 31, 2022 and no exercise of the pre-funded warrants or common warrants issued in this offering.

RISK FACTORS

Investing in our securities 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 securities 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 [Quarterly Report on Form 10-Q for the quarter ended March 31, 2022](#), as applicable, and the factors set out below before deciding to invest in our securities.

Risks related to this offering

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 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 has been, and is likely to continue to be influenced by the following:

- 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;
- 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;
- 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 March 31, 2022, our executive officers, directors, and stockholders who owned more than 5% of our outstanding common stock, in the aggregate, beneficially own shares representing approximately 35.9% 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 securities 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. The perception that such sales or issuances may occur could also negatively impact the market price of our common stock.

We expect that the combined public offering price of our common stock, pre-funded warrants and the accompanying common warrants in this offering will be higher than the net tangible book value per share of our common stock. Therefore, if you purchase shares of our common stock or pre-funded warrants and accompanying common warrants in this offering, you will pay a price per share or pre-funded warrant and accompanying common warrant that substantially exceeds our net tangible book value per share after

this offering. After giving effect to the issuance and sale by us of (i) _____ shares of our common stock and accompanying common warrants to purchase _____ shares of our common stock at a public offering price of \$ _____ per share of common stock and accompanying common warrant and (ii) pre-funded warrants to purchase _____ shares of common stock and accompanying common warrants to purchase _____ shares of our common stock at a public offering price of \$ _____ per pre-funded warrant and accompanying common warrant, our as adjusted net tangible book value as of March 31, 2022 would have been \$ _____ million, or \$ _____ per share, resulting in an immediate increase in the net tangible book value per share of \$ _____ to existing stockholders and an immediate dilution of \$ _____ in net tangible book value per share to investors purchasing securities in this offering, representing the difference between our as adjusted net tangible book value per share after giving effect to this offering and the combined public offering price. To the extent outstanding stock options or warrants are exercised, there will be further dilution to new investors. See “Dilution.”

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 March 31, 2022, 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.

There is no public market for the pre-funded warrants or common warrants to purchase shares of our common stock being offered in this offering.

There is no established public trading market for the pre-funded warrants or the common warrants being offered in this offering, and we do not expect a market to develop. In addition, we do not intend to list the pre-funded warrants or the common warrants, nor do we expect the pre-funded warrants or the common warrants to be quoted, on Nasdaq or any other national securities exchange or any other nationally

recognized trading system. Without an active trading market, the liquidity of the pre-funded warrants and the common warrants will be limited.

Holders of our pre-funded warrants and common warrants will have no rights as a common stockholder until they acquire our common stock.

Until you acquire shares of our common stock upon exercise of the pre-funded warrants or common warrants, you will have no rights with respect to shares of our common stock issuable upon exercise of the pre-funded warrants or common warrants. Upon exercise of your pre-funded warrants or common warrants, you will be entitled to exercise the rights of a common stockholder only as to matters for which the record date occurs after the exercise date.

The pre-funded warrants and common warrants are speculative in nature.

The pre-funded warrants and common warrants offered hereby do not confer any rights of common stock ownership on their holders, such as voting rights or the right to receive dividends, but rather merely represent the right to acquire shares of common stock at a fixed price. Specifically, commencing on the date of issuance, holders of the pre-funded warrants may acquire the common stock issuable upon exercise of such pre-funded warrants at an exercise price of \$ _____ per share and holders of the common warrants may acquire the common stock issuable upon exercise of such common warrants at an exercise price of \$ _____ per share. Moreover, following this offering, the market value of the pre-funded warrants and common warrants is uncertain and there can be no assurance that the market value of the pre-funded warrants or common warrants will equal or exceed their public offering price. There can be no assurance that the market price of the common stock will ever equal or exceed the exercise price of the pre-funded warrants or common warrants and consequently, whether it will ever be profitable for holders of the pre-funded warrants or common warrants to exercise the pre-funded warrants or common warrants.

We may not receive any additional funds upon the exercise of the pre-funded warrants and common warrant.

Each pre-funded warrant and common warrant may be exercised by way of a cashless exercise, meaning that the holder may not pay a cash purchase price upon exercise, but instead would receive upon such exercise the net number of shares of our common stock determined according to the formula set forth in the pre-funded warrant or common warrant, as applicable. Accordingly, we may not receive any additional funds upon the exercise of the pre-funded warrants or common warrants. In addition, the pre-funded warrants have an exercise price of \$ _____ per share of common stock, and as a result we will not receive significant additional funds upon their exercise even if not a cashless exercise.

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

Holders of the pre-funded warrants and common warrants will not be entitled to exercise any portion of any pre-funded warrant or common warrant which, upon giving effect to such exercise, would cause the aggregate number of shares of our common stock beneficially owned by the holder (together with its affiliates) to exceed a specified percentage of the number of shares of our common stock outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the pre-funded warrants and common warrants. As a result, you may not be able to exercise your pre-funded warrants or common warrants for shares of our common stock at a time when it would be financially beneficial for you to do so. In such circumstance you could seek to sell your pre-funded warrants or common warrants to realize value, but you may be unable to do so in the absence of an established trading market for the pre-funded warrants or common warrants.

USE OF PROCEEDS

We estimate that the net proceeds to us from this offering will be approximately \$ _____ million, after deducting underwriting discounts and commissions and estimated offering expenses payable by us and excluding the proceeds, if any, from the exercise of the pre-funded warrants and common warrants issued in this offering. If all the pre-funded warrants are exercised for cash at an exercise price of \$ _____ per share and if all the common warrants are exercised for cash at an exercise price of \$ _____ per share, then our net proceeds will be approximately \$ _____ million, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. We cannot predict when or if the pre-funded warrants or the common warrants will be exercised. It is possible that the pre-funded warrants and common warrants may expire and may never be exercised.

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.

DILUTION

As of March 31, 2022, we had a historical net tangible book value of \$42 million, or \$1.60 per share of common stock, based on 26,215,514 shares of common stock outstanding. Our historical net tangible book value per share represents total tangible assets less total liabilities, divided by the number of shares of common stock outstanding.

After giving effect to the issuance and sale by us of (i) _____ shares of our common stock and accompanying common warrants to purchase _____ shares of our common stock in this offering at a public offering price of \$ _____ per share of common stock and accompanying common warrant and (ii) pre-funded warrants to purchase _____ shares of common stock and accompanying common warrants to purchase _____ shares of our common stock in this offering at a public offering price of \$ _____ per pre-funded warrant and accompanying common warrant, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us and excluding the proceeds and shares issuable, if any, from the exercise of the common warrants issued pursuant to this offering, our as adjusted net tangible book value as of March 31, 2022 would have been \$ _____ million, or \$ _____ per share. This amount represents an immediate increase in our net tangible book value of \$ _____ per share to our existing stockholders and an immediate dilution in our net tangible book value of \$ _____ per share to investors purchasing securities in this offering. We determine dilution by subtracting our as adjusted net tangible book value per share after this offering from the amount of cash paid by an investor for a share of common stock and accompanying common warrant in this offering. The following table illustrates this dilution on a per share basis:

Public offering price per share and accompanying common warrant	\$ _____
Historical net tangible book value per share as of March 31, 2022	\$1.60
increase in net tangible book value per share attributable to investors purchasing securities in this offering	
As adjusted net tangible book value per share after this offering	
Dilution in net tangible book value per share to investors purchasing securities in this offering	\$ _____

The discussion and table above assume no exercise of the common warrants and full exercise of the pre-funded warrants sold in this offering.

The number of shares of our common stock to be outstanding after this offering set forth above is based on 26,215,514 shares of our common stock outstanding as of March 31, 2022 and excludes:

- options to purchase 4,851,565 shares of common stock outstanding under the 2016 Plan and the 2019 Plan;
- restricted stock units to purchase 551,468 shares of common stock outstanding under the 2019 Plan;
- 2,823,766 shares reserved to grant under the 2016 and 2019 Plans and 1,379,543 shares available for future grants under the 2019 Plan;
- 125,618 shares of our common stock issuable upon the exercise of warrants outstanding;
- 487,092 shares of our common stock reserved for future issuance under our 2019 Employee Stock Purchase Plan, or ESPP, as well as any future increases in the number of shares of common stock reserved for issuance under our ESPP; and
- _____ shares of common stock issuable upon exercise of the pre-funded warrants and common warrants issued in this offering.

UNITED STATES FEDERAL INCOME TAX CONSIDERATIONS

The following discussion is a summary of the U.S. federal income tax considerations generally applicable to the ownership and disposition of our common stock, common warrants and pre-funded warrants, which we refer to collectively as our securities. We also refer to the common warrants and pre-funded warrants collectively as warrants. This summary is based upon U.S. federal income tax law as of the date of this prospectus supplement, which is subject to change or differing interpretations, possibly with retroactive effect. This summary does not discuss all aspects of U.S. federal income taxation that may be important to particular investors in light of their individual circumstances, including investors subject to special tax rules (e.g., financial institutions, insurance companies, broker-dealers, tax-exempt organizations (including private foundations), taxpayers that have elected the mark-to-market method of tax accounting, S corporations, regulated investment companies, real estate investment trusts, partnerships, passive foreign investment companies, controlled foreign corporations, investors that will hold our common stock or warrants as part of a straddle, conversion, or other integrated transaction for U.S. federal income tax purposes, expatriates, or investors that have a functional currency other than the U.S. dollar), all of whom may be subject to tax rules that differ materially from those summarized below. In addition, this summary does not discuss other U.S. federal tax consequences (e.g., estate or gift tax), any state, local, or non-U.S. tax considerations or the Medicare tax or alternative minimum tax. In addition, this summary is limited to investors that will hold our securities as “capital assets” (generally, property held for investment) under the Internal Revenue Code of 1986, as amended (the “Code”). No assurance can be given that the IRS would not assert, or that a court would not sustain a position contrary to any of the tax aspects set forth below.

For purposes of this summary, a “U.S. Holder” is a beneficial holder of securities that, for U.S. federal income tax purposes is:

1. an individual who is a United States citizen or resident of the United States;
2. a corporation or other entity treated as a corporation for United States federal income tax purposes created in, or organized under the law of, the United States or any state or political subdivision thereof;
3. an estate the income of which is includible in gross income for United States federal income tax purposes regardless of its source; or
4. a trust (A) the administration of which is subject to the primary supervision of a United States court and which has one or more United States persons (within the meaning of the Code) who have the authority to control all substantial decisions of the trust or (B) that has in effect a valid election under applicable Treasury regulations to be treated as a United States person.

A “non-U.S. Holder” is a beneficial holder of securities that is neither a U.S. Holder nor a partnership for U.S. federal income tax purposes.

THIS DISCUSSION OF U.S. FEDERAL INCOME TAX CONSIDERATIONS IS FOR GENERAL INFORMATION PURPOSES ONLY AND IS NOT TAX ADVICE. PROSPECTIVE HOLDERS SHOULD CONSULT THEIR TAX ADVISORS CONCERNING THE U.S. FEDERAL INCOME TAX CONSEQUENCES TO THEM OF OWNING AND DISPOSING OF OUR SECURITIES, AS WELL AS THE APPLICATION OF ANY, STATE, LOCAL AND NON-U.S. INCOME, ESTATE AND OTHER TAX CONSIDERATIONS.

U.S. Holders

Allocation of Purchase Price Among Shares, Pre-Funded Warrants and Common Warrants

Because our common stock and pre-funded warrants are each sold together with the accompanying common warrants, a purchaser of shares of our common stock or our pre-funded warrants and the accompanying common warrants must allocate its purchase price between each share of our common stock or pre-funded warrant and the accompanying common warrant based on their respective relative fair market values at the time of issuance. This allocation of the purchase price will establish the U.S. Holder’s initial tax basis for U.S. federal income tax purposes for each share of our common stock or pre-funded

warrant and common warrant. A U.S. Holder's allocation of the purchase price is not binding on the IRS or the courts, and no assurance can be given that the IRS or the courts will agree with a U.S. Holder's allocation. Each U.S. Holder should consult its tax advisor regarding the allocation of the purchase price among the shares of common stock or pre-funded warrants and common warrants.

Exercise of a Warrant

Except as discussed below with respect to the cashless exercise of a warrant, a U.S. Holder will not recognize gain or loss upon the exercise of a warrant. The U.S. Holder's tax basis in the share of our common stock received upon exercise of the warrant will generally be an amount equal to the sum of (i) the U.S. Holder's adjusted tax basis in the warrant and (ii) the exercise price of such warrant. A U.S. Holder's adjusted tax basis in a warrant generally is equal to the U.S. Holder's initial investment in the warrant, increased by any constructive distributions that are treated as dividends and decreased by any constructive distributions treated as returns of capital. It is unclear whether a U.S. Holder's holding period for the common stock received upon exercise of the warrant would commence on the date of exercise of the warrant or the day following the date of exercise of the warrant; however, in either case the holding period will not include the period during which the U.S. Holder held the warrants, except in the case of a pre-funded warrant. Because the pre-funded warrants are generally expected to be treated as shares of our common stock for U.S. federal income tax purposes, the holding period for pre-funded warrants may carry over to the common stock received on exercise.

The tax consequences of a cashless exercise of a warrant are not entirely clear under current tax law. A cashless exercise may not be subject to tax, either because the exercise is not a realization event or because the exercise is treated as a recapitalization for U.S. federal income tax purposes. In either situation, a U.S. Holder's tax basis in the common stock received would generally equal the holder's tax basis in the warrant. If the cashless exercise were treated as not being a realization event, it is unclear whether a U.S. Holder's holding period for the common stock would commence on the date of exercise of the warrant or the day following the date of exercise of the warrant. If, however, the cashless exercise were treated as a recapitalization, the holding period of the common stock would include the holding period of the warrant.

It is also possible that a cashless exercise of a common warrant could be treated as a taxable exchange in which gain or loss is recognized. In such event, a U.S. Holder would be deemed to have surrendered a number of common warrants having a value equal to the exercise price. The U.S. Holder would recognize capital gain or loss in an amount equal to the difference between the exercise price of the common warrants deemed exercised and the U.S. Holder's tax basis in the common warrants deemed surrendered. In this case, a U.S. Holder's tax basis in the common stock received would equal the sum of the U.S. Holder's initial investment in the common warrants deemed exercised and the exercise price of such common warrants. It is unclear whether a U.S. Holder's holding period for the common stock would commence on the date of exercise of the common warrant or the day following the date of exercise of the warrant.

Due to the absence of authority on the U.S. federal income tax treatment of a cashless exercise, including when a U.S. Holder's holding period would commence with respect to the common stock received, there can be no assurance which, if any, of the alternative tax consequences and holding periods described above would be adopted by the IRS or a court of law. Accordingly, U.S. Holders are urged to consult their tax advisors regarding the tax consequences of a cashless exercise.

Sale, Exchange or Expiration of a Warrant

Upon a sale, exchange (other than by exercise) or expiration of a warrant, a U.S. Holder will recognize taxable gain or loss in an amount equal to the difference between (1) the amount realized upon such disposition or expiration and (2) the U.S. Holder's tax basis in the warrant. Such gain or loss will generally be treated as long-term capital gain or loss if the warrant is held by the U.S. Holder for more than one year at the time of such disposition or expiration. If a warrant is allowed to lapse unexercised, a U.S. Holder generally will recognize a capital loss equal to such holder's tax basis in the warrant. The deductibility of capital losses is subject to certain limitations.

Possible Constructive Distributions

The terms of each warrant provide for an adjustment to the number of shares of common stock for which the warrant may be exercised or to the exercise price of the warrant in certain events, as discussed in the section of this prospectus supplement captioned “*Description of Warrants — Fundamental Transaction.*” An adjustment which has the effect of preventing dilution is generally not a taxable event. Nevertheless, a U.S. Holder of warrants may be treated as receiving a constructive distribution from us if, for example, the adjustment increases the holder’s proportionate interest in our assets or earnings and profits (e.g., through an increase in the number of shares of common stock that would be obtained upon exercise) as a result of a distribution of cash to the holders of shares of our common stock which is taxable to such holders as a distribution. Such constructive distribution would be subject to tax in the same manner as if such U.S. Holder received a cash distribution from us equal to the fair market value of such increased interest.

Non-U.S. Holders

Distributions on Our Common Stock

We have not paid and do not anticipate paying dividends. However, any dividends we pay to a non-U.S. Holder with respect to shares of our common stock will generally be subject to withholding tax at a 30% rate (or such lower rate specified by an applicable income tax treaty). To obtain the benefit of a reduced rate under an applicable income tax treaty, a non-U.S. Holder must certify as to its non-U.S. status, that no withholding is required pursuant to FATCA (discussed below), and to such right under the applicable income tax treaty on a properly completed IRS Form W-8BEN or IRS Form W-8BEN-E. If, however, a non-U.S. Holder provides an IRS Form W-8ECL, certifying that the dividend is effectively connected with the non-U.S. Holder’s conduct of a trade or business within the U.S. (and, in the case of certain income tax treaties, is attributable to a permanent establishment or fixed base maintained by the non-U.S. holder in the U.S.), the dividend will not be subject to withholding. Instead, such dividends are subject to U.S. federal income tax at regular rates applicable to U.S. persons generally and, for corporate holders, may also be subject to a 30% “branch profits tax” unless the non-U.S. Holder qualifies for a lower rate under an applicable U.S. income tax treaty.

Sale, Exchange or Other Taxable Disposition of Common Stock and Warrants

A non-U.S. Holder will generally not be subject to U.S. federal income or withholding tax in respect of gain recognized on a sale, taxable exchange or other taxable disposition of our common stock or warrants or an expiration of our warrants unless:

- the gain is effectively connected with the conduct of a trade or business by the non-U.S. Holder within the United States (and, if an applicable tax treaty so requires, is attributable to a U.S. permanent establishment or fixed base maintained by the non-U.S. Holder);
- the non-U.S. Holder is an individual who is present in the United States for 183 days or more in the taxable year of disposition and certain other conditions are met; or
- we are or have been a “United States real property holding corporation” for U.S. federal income tax purposes during a specified period and certain other requirements are met. We do not expect to be a “United States real property holding corporation” for U.S. federal income tax purposes, but there can be no assurance in that regard.

Gain described in the first bullet point above will be subject to tax at the generally applicable U.S. federal income tax rates. Any gains described in the first bullet point above of a non-U.S. Holder that is a foreign corporation may also be subject to an additional “branch profits tax” at a 30% rate (or lower applicable treaty rate). Gain described in the second bullet point above will generally be subject to a flat 30% U.S. federal income tax. Non-U.S. Holders are urged to consult their tax advisors regarding possible eligibility for benefits under income tax treaties. If the third bullet point above applies to a non-U.S. Holder, gain recognized by such holder on the sale, exchange or other disposition of our common stock or warrants will be subject to tax at the generally applicable U.S. federal income tax rates, and certain withholding requirements may apply. Non-U.S. Holders are urged to consult their tax advisors regarding the application of these rules.

Allocation of Purchase Price Between Shares or Pre-Funded Warrants and Common Warrants

If it is relevant for a non-U.S. Holder to determine its tax basis in shares of common stock, pre-funded warrants or common warrants for U.S. federal income tax purposes, a non-U.S. Holder will determine such tax basis based on the allocation of the purchase price as described under “*United States Federal Income Tax Considerations — U.S. Holders — Allocation of Purchase Price Between Shares or Pre-Funded Warrants and Common Warrants*” above.

Exercise of a Warrant

The U.S. federal income tax treatment of a non-U.S. Holder’s exercise of a warrant generally will correspond to the U.S. federal income tax treatment of the exercise of a warrant by a U.S. Holder, as described under “*U.S. Holders — Exercise of a Warrant*” above, although to the extent a cashless exercise results in a taxable exchange, the tax consequences to the non-U.S. Holder would be the same as those described below in “*Non-U.S. Holders — Gain on Sale, Exchange or Other Taxable Disposition of Common Stock and Warrants.*”

Possible Constructive Distributions

The terms of each warrant provide for an adjustment to the number of shares of common stock for which the warrant may be exercised or to the exercise price of the warrant in certain events, as discussed in the section of this prospectus captioned “*Description of Warrants — Fundamental Transaction.*” An adjustment which has the effect of preventing dilution is generally not a taxable event. Nevertheless, a non-U.S. Holder of warrants may be treated as receiving a constructive distribution from us if, for example, the adjustment increases the holder’s proportionate interest in our assets or earnings and profits (e.g., through an increase in the number of shares of common stock that would be obtained upon exercise) as a result of a distribution of cash to the holders of shares of our common stock which is taxable to such holders as a distribution. A non-U.S. Holder would be subject to U.S. federal income tax withholding (which may be withheld from any amount paid to or held on behalf of a non-U.S. Holder by an applicable withholding agent) in the same manner as if such non-U.S. Holder received a cash distribution from us equal to the fair market value of such increased interest.

Foreign Account Tax Compliance Act

Under the Foreign Account Tax Compliance Act (“FATCA”), withholding at a rate of 30% will generally be required on dividends in respect of shares of our common stock (or constructive dividends on our warrants) held by or through certain foreign financial institutions (including investment funds), unless such institution (i) enters into an agreement with the U.S. Department of the Treasury to report, on an annual basis, information with respect to shares in, and accounts maintained by, the institution to the extent such shares (or warrants) or accounts are held by certain U.S. persons and by certain non-U.S. entities that are wholly or partially owned by U.S. persons and to withhold on certain payments, or (ii) complies with the terms of an intergovernmental agreement between the United States and an applicable foreign country. Accordingly, the entity through which our common stock or warrants is held will affect the determination of whether such withholding is required. Similarly, dividends in respect of shares of our common stock (or constructive dividends on our warrants) held by an investor that is a non-financial non-U.S. entity that does not qualify under certain exemptions will be subject to withholding at a rate of 30%, unless such entity either (i) certifies that such entity does not have any “substantial United States owners” or (ii) provides certain information regarding the entity’s “substantial United States owners,” which we or the applicable withholding agent will in turn provide to the Secretary of the Treasury. An intergovernmental agreement between the United States and an applicable foreign country, or future Treasury regulations or other guidance, may modify these requirements. We will not pay any additional amounts to investors in respect of any amounts withheld. Non-U.S. investors are encouraged to consult their tax advisors regarding the possible implications of the legislation on their investment in our common stock or warrants.

DESCRIPTION OF WARRANTS

The following is a summary of the material terms and provisions of the pre-funded warrants and common warrants that are being offered hereby. This summary is subject to and qualified in its entirety by the form of warrant, which will be filed with the SEC as an exhibit to a Current Report on Form 8-K in connection with this offering and incorporated by reference into the registration statement of which this prospectus supplement and the accompanying prospectus form a part. Prospective investors should carefully review the terms and provisions of the form of warrant for a complete description of the terms and conditions of the pre-funded warrants and common warrants.

Duration and Exercise Price. The pre-funded warrants offered hereby will have an exercise price of \$ _____ per share and will expire on the _____-year anniversary of the date of issuance. The common warrants offered hereby will have an exercise price of \$ _____ per share and will expire on the _____-year anniversary of the date of issuance. The exercise price and number of shares of common stock issuable upon exercise of the pre-funded warrants and common warrants are subject to appropriate adjustment in the event of stock dividends, stock splits, reorganizations or similar events affecting our common stock.

Exercisability. The pre-funded warrants and common warrants will be exercisable, at the option of each holder, in whole or in part, by delivering a duly executed exercise notice accompanied by payment in full for the number of shares of our common stock purchased upon such exercise (except in the case of a cashless exercise as discussed below). A holder (together with its affiliates) may not exercise any portion of such holder's pre-funded warrants or common warrants to the extent that the holder would beneficially own more than 9.99% of our outstanding common stock immediately after exercise, other than in the case of a holder (together with its affiliates) who immediately prior to the issue date of the pre-funded warrants and common warrants beneficially owns more than 9.99% of our outstanding common stock at such time, in which case that holder may not exercise any portion of such holder's pre-funded warrants or common warrants to the extent that the holder (together with its affiliates) would beneficially own more than 19.99% of our outstanding common stock immediately after exercise.

Exercise Limitations. We may not effect the exercise of any pre-funded warrant or common warrant, and a holder will not be entitled to exercise any portion of any pre-funded warrant or common warrant that, upon giving effect to such exercise, would cause the aggregate number of shares of common stock beneficially owned by such holder (together with its affiliates) to exceed 9.99% of the number of shares of common stock outstanding immediately after giving effect to the exercise. However, in the case of a holder (together with its affiliates) who immediately prior to the issue date of the pre-funded warrants and common warrants beneficially owns more than 9.99% of our outstanding common stock at such time, that holder may not exercise any portion of such holder's pre-funded warrants or common warrants to the extent that the holder (together with its affiliates) would beneficially own more than 19.99% of our outstanding common stock immediately after exercise.

Cashless Exercise. If, at the time a holder exercises its pre-funded warrants or common warrants a registration statement registering the issuance of the shares of common stock underlying such pre-funded warrants or common warrants under the Securities Act is not then effective or available for the issuance of such shares, or the prospectus contained therein is not available for the issuance of such shares, then in lieu of making the cash payment to us upon such exercise in payment of the aggregate exercise price, the holder may elect instead to receive upon such exercise (either in whole or in part) the net number of shares of common stock determined according to a formula set forth in the pre-funded warrants and common warrants.

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

Trading Market. There is no established trading market for any of the pre-funded warrants or common warrants, and we do not expect a market to develop. We do not intend to apply for a listing for any of the pre-funded warrants or common warrants on any securities exchange or other nationally recognized trading system. Without an active trading market, the liquidity of the pre-funded warrants and the common warrants will be limited.

Rights as a Shareholder. Except as otherwise provided in the pre-funded warrants or the common warrants or by virtue of the holders' ownership of shares of our common stock, the holders of pre-funded

warrants and the common warrants do not have the rights or privileges of the holders of our common stock, including any voting rights, until such warrant holders exercise their pre-funded warrants or common warrants.

Fundamental Transaction. In the event of a fundamental transaction, as described in the pre-funded warrants and the common warrants and generally including any reorganization, recapitalization or reclassification of our common stock, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, the acquisition of 50% or more of our outstanding common stock, or any person or group becoming the beneficial owner of 50% or more of the voting power represented by our outstanding common stock, the holders of the pre-funded warrants and the common warrants will be entitled to receive, upon exercise of the pre-funded warrants or the common warrants, the kind and amount of securities, cash or other property that such holders would have received had they exercised the pre-funded warrants or the common warrants immediately prior to such fundamental transaction, without regard to any limitations on exercise contained in the pre-funded warrants or the common warrants. In the event of a change of control that is approved by the company's board of directors, the holders of the pre-funded warrants and the common warrants shall be entitled to receive from the company or any successor entity, as of the date of consummation of the change of control, the same type or form of consideration (and in the same proportion), at the Black Scholes Value of the unexercised portion of the pre-funded warrants or the common warrants, that is being offered and paid to the holders of common stock of the company in connection with the change of control, whether that consideration be in the form of cash, stock, or any combination thereof, or whether the holders of common stock are given the choice to receive from among alternative forms of consideration in connection with the change of control.

UNDERWRITING

SVB Securities LLC is acting as the sole book-running manager for this offering. Subject to the terms and conditions set forth in the underwriting agreement dated the date of this prospectus supplement, we have agreed to sell to the underwriter, and the underwriter has agreed to purchase from us, the number of shares of common stock, pre-funded warrants and accompanying common warrants set forth opposite its name below.

Underwriter	Number of Shares of Common Stock	Number of Pre-Funded Warrants	Number of Shares Underlying Accompanying Common Warrants
SVB Securities LLC			
Total	=====	=====	=====

Subject to the terms and conditions set forth in the underwriting agreement, the underwriter has agreed to purchase all of the shares, pre-funded warrants and accompanying common warrants sold under the underwriting agreement if any of the shares or pre-funded warrants and accompanying common warrants are purchased. If the underwriter defaults, the underwriting agreement provides that the underwriting agreement may be terminated.

We have agreed to indemnify the underwriter against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriter may be required to make in respect of those liabilities.

The underwriter is offering the shares, pre-funded warrants and accompanying common warrants, subject to prior sale, when, as and if issued to and accepted by it, subject to approval of legal matters by its counsel, including the validity of the shares, pre-funded warrants and accompanying common warrants, and subject to other conditions contained in the underwriting agreement, such as the receipt by the underwriter of officers' certificates and legal opinions. The underwriter reserves the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Discounts and Commissions

The underwriter proposes initially to offer the shares, pre-funded warrants and accompanying common warrants to the public at the public offering prices set forth on the cover page of this prospectus supplement and to dealers at those prices less a concession not in excess of \$ per share and accompanying common warrant and \$ per pre-funded warrant and accompanying common warrant. After the initial offering of the shares, pre-funded warrants and accompanying common warrants, the public offering prices, concessions or any other term of this offering may be changed by the underwriter.

The following table shows the public offering prices, underwriting discounts and commissions and proceeds, before expenses, to us.

	Per Share and Accompanying Common Warrant	Per Pre-Funded Warrant and Accompanying Common Warrant	Total
Public offering price	\$	\$	\$
Underwriting discounts and commissions	\$	\$	\$
Proceeds, before expenses, to us	\$	\$	\$

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately \$. We also have agreed to reimburse the underwriter for up to \$30,000 for their FINRA counsel fee. In accordance with FINRA Rule 5110, this reimbursed fee is deemed underwriting compensation for this offering.

No Sales of Similar Securities

We, our officers and directors, and certain holders of more than 5% of our outstanding shares of common stock, or securities convertible into or exchangeable for shares of our common stock, have agreed

that, for a period of 60 days from the date of this prospectus, or the restricted period, we and they will not, without the prior written consent of the representatives, dispose of or hedge any shares or any securities convertible into or exchangeable for our common stock.

With respect to us, the restrictions described above are subject to specified exceptions including the:

- sale of shares, pre-funded warrants and accompanying common warrants to the underwriter;
- issuance and sale of shares of common stock or securities convertible into, or exercisable or exchangeable for, shares of common stock, pursuant to any employee stock option plan, stock ownership plan, dividend reinvestment plan or any other plan or arrangement described in this prospectus;
- issuance of the pre-funded warrants and common warrants sold in this offering, the shares of common stock underlying those pre-funded warrants and common warrants and shares of common stock upon the conversion of securities outstanding as of the date of this prospectus, or the exercise of warrants or options or the settlement of restricted stock units outstanding as of the date of this prospectus or issued thereafter pursuant to any employee stock option plan or similar plan described above; filing of one or more registration statements on Form S-8 relating to any employee stock option plan or similar plan described above; and
- issuance of, or the entry into an agreement to issue, shares of common stock, or securities convertible into, exercisable or exchangeable for shares of common stock, in connection with any merger, joint venture, strategic alliance or partnership; provided that the aggregate number of shares of common stock, or securities convertible or exercisable or exchangeable for shares of common stock, so issued does not exceed 5.0% of the total shares of common stock outstanding immediately following the issuance of shares in this offering, and the recipients of any such securities provide the representatives with a lock-up agreement containing the restrictions described above.

With respect to our officers and directors, and holders of more than 5% of our outstanding shares of common stock, the restrictions described above are subject to specified exceptions, including for any transfer of shares of common stock or any security convertible into or exercisable or exchangeable for common stock, subject to certain requirements:

- as a bona fide gift;
- by will, testamentary document or intestate succession upon the death of the officer, director or stockholder to the legal representative, heir, beneficiary or a member of the immediate family of the officer, director or stockholder;
- to an immediate family member of the officer, director or stockholder or to any trust for the direct or indirect benefit of the officer, director or stockholder or their immediate family;
- if the stockholder is a trust, to a trustor, trustee or beneficiary of the trust or to the estate of a trustor, trustee or beneficiary of such trust;
- as a distribution by a partnership to its limited or general partners or by a limited liability company to its members or by a corporation to its stockholders or to any wholly owned subsidiary of such corporation or by any other entity to its equityholders;
- to any affiliate of the stockholder, or any investment fund or other entity under common control or management by entities that are affiliates of the stockholder;
- pursuant to a domestic order or negotiated divorce settlement;
- in connection with the withholding of shares by, or surrender of shares to, us to cover the payment of taxes due upon or consideration required in connection with the vesting, conversion or exercise of securities issued under our equity incentive or stock purchase plans described in this prospectus, or pursuant to a “net” or “cashless” exercise or settlement feature;
- transfers under an existing trading plan pursuant to Rule 10b5-1 under the Exchange Act;
- transfers related to shares of common stock acquired in this offering or in open market transactions after the completion of this offering;

- transfers in connection with the termination of the employment with us or pursuant to contractual arrangements under which we have the option to repurchase such shares;
- the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of shares of common stock; provided that such plan does not provide for any transfers of shares of common stock during the restricted period;
- the exercise, vesting or settlement of any option to purchase any shares of common stock or other equity awards pursuant to any stock incentive plan or stock purchase plan described in this prospectus; and
- transfers pursuant to a bona fide third-party tender offer, merger, consolidation or other similar transaction made to all holders of our common stock involving a change of control that has been approved by our board of directors.

The representatives in their sole discretion may release any of the securities subject to these lock-up agreements at any time, which, in the case of officers and directors, shall be with notice.

Nasdaq Global Market Listing

Our common stock is listed on Nasdaq under the symbol “APLT.” There is no established public trading market for the pre-funded warrants or the common warrants, and we do not expect a market to develop. In addition, we do not intend to list the pre-funded warrants or the common warrants, nor do we expect the pre-funded warrants or the common warrants to be quoted, on Nasdaq or any other national securities exchange or any other nationally recognized trading system. Without an active trading market, the liquidity of the pre-funded warrants and the common warrants will be limited.

Price Stabilization, Short Positions and Penalty Bids

Until the distribution of the securities is completed, SEC rules may limit the underwriter and selling group members from bidding for and purchasing our common stock. However, the underwriter may engage in transactions that stabilize the price of the common stock, such as bids or purchases to peg, fix or maintain that price.

In connection with this offering, the underwriter may purchase and sell our common stock in the open market. These transactions may include short sales, purchases on the open market to cover positions created by short sales and stabilizing transactions. Short sales involve the sale by the underwriter of a greater number of shares than they are required to purchase in this offering. Stabilizing transactions consist of various bids for or purchases of shares of common stock made by the underwriter in the open market prior to the closing of this offering.

The underwriter may also impose a penalty bid. This occurs when an underwriter repays a portion of the underwriting discount received by it because it has repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Similar to other purchase transactions, the underwriter’s purchases to cover syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. The underwriter may conduct these transactions on Nasdaq, in the over-the-counter market or otherwise.

Neither we nor the underwriter make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. In addition, neither we nor the underwriter make any representation that the representatives will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

The underwriter may also engage in passive market making transactions in our common stock on Nasdaq in accordance with Rule 103 of Regulation M during a period before the commencement of offers or sales of shares of our common stock and accompanying warrants in this offering and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the

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

Electronic Distribution

In connection with this offering, the underwriter or securities dealers may distribute prospectuses by electronic means, such as e-mail.

Other Relationships

The underwriter and certain of its affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriter and certain of its affiliates may in the future engage in investment banking and other commercial dealings in the ordinary course of business with us and our affiliates, for which they may in the future receive customary fees, commissions and expenses.

In addition, in the ordinary course of their business activities, the underwriter and its affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriter 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

Notice to Prospective Investors in the European Economic Area

In relation to each Member State of the European Economic Area (each, a "Relevant State"), no securities 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 securities 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 securities may be offered to the public in that Relevant State at any time:

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

provided that no such offer of securities shall require us or any of the representatives to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation.

For the purposes of this provision, the expression an "offer to the public" in relation to any securities 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 securities to be offered so as to enable an investor to decide to purchase or subscribe for any securities, and the expression "Prospectus Regulation" means Regulation (EU) 2017/1129, as amended.

Notice to Prospective Investors in the United Kingdom

No securities have been offered or will be offered pursuant to the offering to the public in the United Kingdom prior to the publication of a prospectus in relation to the securities which has been

approved by the Financial Conduct Authority, except that the securities may be offered to the public in the United Kingdom at any time:

- A. to any legal entity which is a qualified investor as defined under Article 2 of the UK Prospectus Regulation;
- B. to fewer than 150 natural or legal persons (other than qualified investors as defined under Article 2 of the UK Prospectus Regulation), subject to obtaining the prior consent of the representatives for any such offer; or
- C. in any other circumstances falling within Section 86 of the Financial Services and Markets Act 2000 (the “FSMA”),

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

Notice to Prospective Investors in Canada

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

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

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

Notice to Prospective Investors in Australia

This document does not constitute a prospectus, product disclosure statement or other disclosure document under the Australia’s Corporations Act 2001 (Cth) (the “Corporations Act”) of Australia. This document has not been lodged with the Australian Securities & Investments Commission and is only directed to the categories of exempt persons set out below. Accordingly, if you receive this document in Australia:

You confirm and warrant that you are either:

- a “sophisticated investor” under section 708(8)(a) or (b) of the Corporations Act;
- a “sophisticated investor” under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant’s certificate to the company which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made; or
- a “professional investor” within the meaning of section 708(11)(a) or (b) of the Corporations Act.

To the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor or professional investor under the Corporations Act any offer made to you under this document is void and incapable of acceptance.

You warrant and agree that you will not offer any of the shares or warrants issued to you pursuant to this document for resale in Australia within 12 months of those securities being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

Notice to Prospective Investors in Hong Kong

No securities have been, may be or will be offered or sold in Hong Kong, by means of any document, other than to persons whose ordinary business is to buy or sell shares or debentures, whether as principal or agent; or to “professional investors” as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong (the “SFO”) and any rules made thereunder; or in other circumstances which do not result in the document being a “prospectus” as defined in the Companies (Winding UP and Miscellaneous Provisions) Ordinance (Cap. 32) of Hong Kong (the “C(WUMP)O”), or which do not constitute an offer to the public within the meaning of the C(WUMP)O. No document, invitation or advertisement relating to the securities has been issued or may be issued or will 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 of Hong Kong (except if permitted under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to “professional investors” as defined in the SFO and any rules made thereunder.

This document has not been and will not be registered with the Registrar of Companies in Hong Kong. Accordingly, this document may not be issued, circulated or distributed in Hong Kong, and the securities may not be offered for subscription to members of the public in Hong Kong. Each person acquiring the securities will be required, and is deemed by the acquisition of the securities, to confirm that he is aware of the restriction on offers of the securities described in this document and the relevant offering documents and that he is not acquiring, and has not been offered any securities in circumstances that contravene any such restrictions.

Notice to Prospective Investors in Japan

The offering has not been and will not be registered under the Financial Instruments and Exchange Act of Japan (Act No. 25 of 1948 of Japan, as amended) (the “FIEA”), and the underwriter will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means, unless otherwise provided herein, any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the FIEA and any other applicable laws, regulations and ministerial guidelines of Japan.

Notice to Prospective Investors in Singapore

This document has not been and will not be lodged or registered with the Monetary Authority of Singapore. Accordingly, this document and any other document or material in connection with the offer or sale, or the invitation for subscription or purchase of the securities may not be issued, circulated or distributed, nor may the securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to any person in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the “SFA”), (ii) to a relevant person as defined under Section 275(2) 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 and where (where applicable) Regulation 3 of the Securities and Futures (Classes of Investors) Regulations 2018, or (iii) otherwise pursuant to, and in accordance with the conditions of any other applicable provision of the SFA. **In the event that you are not an investor falling within any of the categories set out above, please return this document immediately. You may not forward or circulate this document to any other person in Singapore.**

No offer is made to you with a view to the securities being subsequently offered for sale to any other party. There are on-sale restrictions that may be applicable to investors who acquire securities. As such, investors are advised to acquaint themselves with the provisions of the SFA relating to resale restrictions and comply accordingly.

Where the securities 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 under Section 4A of the SFA) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor,

securities or securities-based derivatives contracts (each term as defined in Section 2(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferable within six months after that corporation or that trust has acquired the securities under Section 275 of the SFA except:

- to an institutional investor under Section 274 of the SFA or to a relevant person defined in Section 275(2) of the SFA, or to any person pursuant to an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;
- where no consideration is given for the transfer;
- where the transfer is by operation of law;
- as specified in Section 276(7) of the SFA; or
- as specified in Regulation 37A of the Securities and Futures (Offers of Investments) (Securities and Securities-based Derivatives Contracts) Regulations 2018 of Singapore.

Notice to Prospective Investors in Switzerland

The securities may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This document has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the securities or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, the issuer or the securities have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, or FINMA, and the offer of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of securities.

Notice to Prospective Investors in Israel

This document does not constitute a prospectus under the Israeli Securities Law, 5728-1968, or the Securities Law, and has not been filed with or approved by the Israel Securities Authority. In the State of Israel, this document is being distributed only to, and is directed only at, and any offer of the shares or warrants is directed only at, investors listed in the first addendum, or the Addendum, to the Israeli Securities Law, consisting primarily of joint investment in trust funds, provident funds, insurance companies, banks, portfolio managers, investment advisors, members of the Tel Aviv Stock Exchange, underwriters, venture capital funds, entities with equity in excess of NIS 50 million and "qualified individuals", each as defined in the Addendum (as it may be amended from time to time), collectively referred to as qualified investors (in

each case purchasing for their own account or, where permitted under the Addendum, for the accounts of their clients who are investors listed in the Addendum). Qualified investors will be required to submit written confirmation that they fall within the scope of the Addendum, are aware of the meaning of same and agree to it.

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 underwriter 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, 2021](#), as set forth in their report which contains an explanatory paragraph describing conditions that raise substantial doubt about our ability to continue as a going concern as described in Note 1 to the financial statements, 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

Applied Therapeutics, Inc.



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

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

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

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

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

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.

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.

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. 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 66²/₃% of the outstanding voting stock that is not owned by the interested stockholder.

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

- any merger or consolidation involving the corporation and the interested stockholder;

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

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

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

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

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

- permit our board of directors to issue up to 10,000,000 shares of preferred stock, with any rights, preferences and privileges as they may designate, including the right to approve an acquisition or other change in control;
- provide that the authorized number of directors may be changed only by resolution of our board of directors;
- provide that our board of directors be classified into three classes of directors;
- provide that, subject to the rights of any series of preferred stock to elect directors, directors may only be removed for cause, which removal may be effected, subject to any limitation imposed by law, by the holders of at least sixty-six and two-thirds percent (66 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 depository 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 depository for such global security to a nominee of such depository or by a nominee of such depository to such depository or another nominee of such depository or by such depository or any such nominee to a successor of such depository 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.

Shares
Pre-Funded Warrants to Purchase up to **Shares**
Warrants to Purchase up to **Shares**



Applied Therapeutics, Inc.

Common Stock

**Preliminary Prospectus
Supplement**

Sole Book-Running Manager

SVB Securities

, 2022
