

PROSPECTUS SUPPLEMENT
(To Prospectus dated October 19, 2020)

\$5,040,000



Plus Therapeutics, Inc.

Common Stock

On October 23, 2020, we entered into a sales agreement with Canaccord Genuity LLC, or Canaccord, relating to shares of our common stock offered by this prospectus supplement and the accompanying prospectus. In accordance with the terms of the sales agreement, we may offer and sell shares of our common stock having an aggregate offering price of up to \$10,000,000 from time to time through or to Canaccord acting as our sales agent or principal. We previously filed a prospectus supplement offering shares of our common stock having an aggregate offering price of up to \$4,960,000. This prospectus supplement is offering shares of our common stock having an aggregate offering price of \$5,040,000.

Our common stock is listed on the Nasdaq Capital Market under the symbol "PSTV." On February 19, 2021, the last reported sale price of our common stock on the Nasdaq Capital Market was \$3.61 per share.

Sales of our common stock, if any, under this prospectus supplement and the accompanying prospectus will be made in sales deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended, or the Securities Act. Canaccord is not required to sell any specific amount of securities, but will act as our sales agent using commercially reasonable efforts consistent with its normal trading and sales practices, on mutually agreed terms between Canaccord and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

The compensation to Canaccord for sales of common stock sold pursuant to the sales agreement will be an amount equal to 3.0% of the gross proceeds of any shares of common stock sold under the sales agreement. In connection with the sale of the common stock on our behalf, Canaccord will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of Canaccord will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to Canaccord with respect to certain liabilities, including liabilities under the Securities Act or the Securities Exchange Act of 1934, as amended.

The aggregate market value of our outstanding common stock held by non-affiliates is \$34,237,455, based on 9,129,988 shares of outstanding common stock held by non-affiliates as of February 18, 2021 and a price per share of \$3.75, the closing price of our common stock on February 10, 2021. Pursuant to General Instruction I.B.6 of Form S-3, in no event will we sell securities in a public primary offering with a value exceeding more than one-third of our public float in any 12-month period so long as our public float remains below \$75.0 million. We have sold \$4,958,189 in shares of our common stock pursuant to General Instruction I.B.6 of Form S-3 during the prior 12-calendar-month period that ends on, and includes, the date of this prospectus supplement.

Investing in our common stock involves risks. See the section entitled "[Risk Factors](#)" beginning on page S-5 of this prospectus supplement and in the documents we incorporate by reference into this prospectus supplement and the accompanying prospectus.

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

Canaccord Genuity

The date of this prospectus supplement is February 23, 2021

TABLE OF CONTENTS

	<u>Page</u>
Prospectus Supplement	
ABOUT THIS PROSPECTUS SUPPLEMENT	S-1
PROSPECTUS SUPPLEMENT SUMMARY	S-2
THE OFFERING	S-4
RISK FACTORS	S-5
FORWARD-LOOKING STATEMENTS	S-8
USE OF PROCEEDS	S-10
DILUTION	S-11
PLAN OF DISTRIBUTION	S-13
LEGAL MATTERS	S-14
EXPERTS	S-14
WHERE YOU CAN FIND MORE INFORMATION	S-14
INCORPORATION BY REFERENCE	S-15
Prospectus	
ABOUT THIS PROSPECTUS	1
RISK FACTORS	1
PLUS THERAPEUTICS, INC.	1
FORWARD-LOOKING STATEMENTS	2
USE OF PROCEEDS	2
DESCRIPTION OF DEBT SECURITIES	3
DESCRIPTION OF CAPITAL STOCK	9
DESCRIPTION OF DEPOSITARY SHARES	13
DESCRIPTION OF WARRANTS	16
DESCRIPTION OF RIGHTS	16
FORMS OF SECURITIES	17
PLAN OF DISTRIBUTION	19
LEGAL MATTERS	20
EXPERTS	20
WHERE YOU CAN FIND MORE INFORMATION	21
INCORPORATION BY REFERENCE	21

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 also supplements and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part is the accompanying prospectus, which provides more general information, some of which may not apply to this offering. If the information contained in this prospectus supplement differs or varies from the information contained in the accompanying prospectus, you should rely on the information set forth in this prospectus supplement.

You should rely only on the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. We have not, and Canaccord has not, authorized anyone else to provide you with information that is in addition to or different from that contained or incorporated by reference in this prospectus supplement and the accompanying prospectus, along with the information contained in any permitted free writing prospectuses we have authorized for use in connection with this offering.

We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus supplement and the accompanying prospectus is accurate only as of the date of this prospectus supplement or the date of the accompanying prospectus, and the information in the documents incorporated by reference in this prospectus supplement and the accompanying prospectus is accurate only as of the date of those respective documents, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or of any sale of our common stock. Our business, financial condition, results of operations and prospects may have changed since those dates. It is important for you to read and consider all information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus in making your investment decision. You should read both this prospectus supplement and the accompanying prospectus, as well as the documents incorporated by reference into this prospectus supplement and the accompanying prospectus and the additional information described under “Where You Can Find More Information” in this prospectus supplement and in the accompanying prospectus, before investing in our common stock.

All references in this prospectus supplement to “Plus,” the “company,” “we,” “us” and “our” refer to Plus Therapeutics, Inc. and its consolidated subsidiaries, except where the context otherwise requires or as otherwise indicated.

“Plus Therapeutics,” “PSTV” and the Plus logo are our trademarks. This prospectus supplement and the documents incorporated by reference into this prospectus supplement may also contain trademarks and trade names that are the property of their respective owners. We do not intend our use or display of other companies’ trade names, trademarks or service marks to imply relationships with, or endorsements or sponsorship of us by, these other companies.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights certain information about us and this offering. Because it is a summary, it does not contain all of the information that you should consider before investing. Before investing in our common stock, you should read this entire prospectus supplement and the accompanying prospectus carefully, including the "Risk Factors," and the financial statements and accompanying notes and other information incorporated by reference in this prospectus supplement and the accompanying prospectus.

Our Company

Plus Therapeutics is committed to developing and delivering innovative treatments for rare and difficult to treat cancers, with a focus on cancers of the central nervous system. Plus Therapeutics' mission is to transform the clinical care of cancer patients through its innovative drugs that have the potential to improve survival and quality of life.

We have a nanoscale drug development platform and the requisite expertise to innovate and produce new and better therapeutics for rare cancers. We believe that this approach will produce investigational drugs that provide unique benefits such as improved mechanism of action, better tumor targeting, improved pharmacokinetics and higher treatment doses to the tumor. Benefits such as these may then improve the overall efficacy of drugs while reducing the side effects associated with more traditional drug delivery methods. To support this goal, we have an established, GMP-validated nanoscale drug R&D and commercial scale manufacturing facility in San Antonio, TX. This facility is suited to support our efforts to produce nanoliposomal drug candidates for research, development, clinical and commercial use.

As part of our strategy to leverage our nanotechnology platform and expertise, we use a simple multi-step model that management believes allows us to best address unmet market needs or underserved medical conditions while managing risks and minimizing development costs. This model includes: (1) market landscape mapping, (2) internal drug redesign, (3) in house drug manufacturing, (4) performance of critical non-clinical (i.e. bench, animal) analyses, (5) scale-up manufacturing for commercial purposes and performance of early-stage clinical trials, and (6) partnering for late-stage clinical trials, regulatory approval, and, ultimately, commercial launch.

We currently have four investigational drugs, three of which are at the clinical stage for rare and difficult to treat cancers. The three clinical stage drugs in our pipeline are:

- 1) Rhenium NanoLiposomes (RNL™), a patented radiotherapy for patients with recurrent glioblastoma (rGBM) that is currently being evaluated in the U.S. NCI-supported, multi-center ReSPECT™ Phase 1 dose-finding clinical trial;
- 2) DocePLUS™, a patented chemotherapy for patients with solid tumors that has been evaluated in a completed U.S. single-center Phase 1 clinical trial; and
- 3) DoxoPLUS™, a generic chemotherapy that has been evaluated in a completed, bioequivalence clinical trial in the U.S., Canada, and Ukraine versus Janssen's CAELYX® in patients with ovarian cancer.

In addition, we have an early preclinical investigational drug which is a proprietary combination of Rhenium Nanopoliposomes and liposomal doxorubicin. Theoretically, this combination could provide a synergistic combination of both chemotherapy and radiation in a single treatment.

Current business activities related to both DocePLUS and DoxoPLUS are focused on identification of potential partners for these two drugs.

Plus Therapeutics' lead investigational drug, RNL™, is a novel injectable radiotherapy designed to deliver targeted high dose radiation directly into a brain tumor in a safe, effective, and convenient manner to

optimize patient outcomes. RNL™, which is composed of radionuclide Rhenium-186 (¹⁸⁶Re) and a nanoliposomal carrier, is infused directly into the brain tumor via precision brain mapping and convection enhanced delivery. The RNL radiation dose delivered to patients may be up to 15-20x greater than what is possible with external beam radiation therapy (EBRT). In September 2020, the FDA granted both Orphan Drug designation and Fast Track designation to RNL for the treatment of patients with glioblastoma. Current business activities related to both DocePLUS and DoxoPLUS are focused on identification of potential partners for these two drugs.

Corporate Information

We were initially formed as a California general partnership in July 1996 and incorporated in the State of Delaware in May 1997. We were formerly known as Cytori Therapeutics, Inc., before that as MacroPore Biosurgery, Inc. and before that as MacroPore, Inc. On July 20, 2019 we changed our name from Cytori Therapeutics, Inc. to Plus Therapeutics, Inc. Our corporate offices are located at 4200 Marathon Blvd., Suite 200, Austin, Texas 78756. Our telephone number is (737) 255-7194. We maintain a website at www.plustherapeutics.com. The contents of our website are not part of this prospectus supplement and the references in this prospectus supplement, the accompanying prospectus and the documents we have incorporated by reference to our website do not constitute incorporation by reference into this prospectus supplement or the accompanying prospectus of the information contained therein.

THE OFFERING

Common stock offered	Shares of our common stock having an aggregate offering price of up to \$5,040,000.
Manner of offering	“At the market offering” that may be made from time to time through our sales agent, Canaccord Genuity LLC. See “Plan of Distribution” on page S-13 of this prospectus supplement.
Use of proceeds	We intend to use the net proceeds from this offering for general corporate purposes and working capital. We may also use a portion of the net proceeds from this offering to acquire or invest in complementary businesses, technologies, product candidates or other intellectual property, although we have no present commitments or agreements to do so. See “Use of Proceeds” on page S-10 of this prospectus supplement.
Risk factors	See “Risk Factors” beginning on page S-5 of this prospectus supplement, and under similar headings in other documents filed after the date hereof and incorporated by reference into this prospectus supplement and the accompanying prospectus, for a discussion of factors you should consider carefully before deciding to invest in our common stock.
Nasdaq Capital Market symbol	“PSTV”

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before making an investment decision, you should carefully consider the risks described below and in our Annual Report on Form 10-K for the year ended December 31, 2020, as amended, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K incorporated by reference in this prospectus supplement and the accompanying prospectus, any amendment or update thereto reflected in our subsequent filings with the SEC, and all of the other information in this prospectus supplement and the accompanying prospectus, including our financial statements and related notes incorporated by reference in this prospectus supplement and the accompanying prospectus. If any of these risks is realized, our business, financial condition, results of operations and prospects could be materially and adversely affected. In that event, the trading price of our common stock could decline and you could lose part or all of your investment. Additional risks and uncertainties that are not yet identified or that we think are immaterial may also materially harm our business, operating results and financial condition and could result in a complete loss of your investment.

Risks Related to this Offering

The report of our independent registered public accounting firm contains an emphasis paragraph regarding the substantial doubt about our ability to continue as a “going concern.”

The audit report of our independent registered public accounting firm covering the December 31, 2020 consolidated financial statements contains an explanatory paragraph that states that our recurring losses from operations, liquidity position, and debt service requirements raises substantial doubt about our ability to continue as a going concern. This going concern opinion could materially limit our ability to raise additional funds through the issuance of new debt or equity securities or otherwise. Future reports on our financial statements may also include an explanatory paragraph with respect to our ability to continue as a going concern. To date, our operating losses have been funded primarily from outside sources of invested capital and gross profits. We have had, and we will likely continue to have, an ongoing need to raise additional cash from outside sources to fund our future operations. However, no assurance can be given that additional capital will be available when required or on terms acceptable to us. If we are unsuccessful in our efforts to raise any such additional capital, we may be required to take actions that could materially and adversely harm our business, including a possible significant reduction in our research, development and administrative operations (including reduction of our employee base), the surrender of our rights to some technologies or product opportunities, delay of our clinical trials or regulatory and reimbursement efforts, or the curtailment or cessation of operations. We also cannot give assurance that we will achieve sufficient revenues in the future to achieve profitability and cash flow positive operations to allow us to continue as a going concern. The perception that we may not be able to continue as a going concern may cause third parties to choose not to deal with us due to concerns about our ability to meet our contractual obligations, which could have a material adverse effect on our business.

Purchasers in this offering will experience immediate and substantial dilution in the book value of their investment.

The common stock sold in this offering from time to time will be sold at various prices; however, we expect the price per share of common stock will be substantially higher than the net tangible book value of our common stock. Therefore, purchasers of our common stock in this offering will experience immediate dilution in the net tangible book value of the common stock purchased in this offering. Assuming that an aggregate of 1,396,122 shares of common stock are sold at a public offering price of \$3.61 per share, the last reported sale price of our common stock on the Nasdaq Capital Market on February 19, 2021, for an aggregate gross proceeds of \$5,040,000 and after deducting estimated commissions and estimated offering expenses payable by us, our adjusted net tangible book value as of December 31, 2020, would have been approximately \$7.3 million, or approximately \$0.90 per share of our common stock. As a result, if you purchase shares of common stock in this offering at that assumed public offering price, you will suffer immediate and substantial dilution of

approximately \$2.71 per share with respect to the net tangible book value of the common stock. See “Dilution” in this prospectus supplement for a detailed illustration of the dilution you will incur if you purchase shares in this offering.

Our management will have broad discretion over the use of the net proceeds from our sale of shares of common stock in this offering, and you may not agree with how we use the proceeds and the proceeds may not be invested successfully.

Although we currently intend to use the net proceeds from this offering in the manner described in the section entitled “Use of Proceeds” in this prospectus supplement, our management will have broad discretion as to the use of the net proceeds from our sale of shares in this offering, and we could use them for purposes other than those contemplated at the time of commencement of this offering. Accordingly, you will be relying on the judgment of our management with regard to the use of those net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. It is possible that, pending their use, we may invest those net proceeds in a way that does not yield a favorable, or any, return for us. The failure of our management to use such funds effectively could have a material adverse effect on our business, financial condition, operating results and cash flows.

Future sales of our common stock could cause dilution, and the sale of such common stock, or the perception that such sales may occur, could cause the price of our stock to decline.

Sales of additional shares of our common stock, as well as securities convertible into or exercisable for common stock, could result in substantial dilution to our stockholders and cause the market price of our common stock to decline. An aggregate of 6,749,028 shares of common stock were outstanding as of December 31, 2020. As of such date, another 3,991,821 shares of common stock were issuable upon exercise of outstanding options and warrants and the conversion of outstanding shares of preferred stock. A substantial majority of the outstanding shares of our common stock, as well as a substantial majority of the shares of common stock issuable upon exercise of outstanding options, are freely tradable without restriction or further registration under the Securities Act.

We may sell additional shares of common stock, as well as securities convertible into or exercisable for common stock, in subsequent public or private offerings. We may also issue additional shares of common stock, as well as securities convertible into or exercisable for common stock, to finance future acquisitions. We will need to raise additional capital in order to initiate or complete additional development activities for all of our product candidates, or to pursue additional disease indications for our product candidates, and this may require us to issue a substantial amount of securities (including common stock as well as securities convertible into or exercisable for common stock). There can be no assurance that our capital raising efforts will be able to attract the capital needed to execute on our business plan and sustain our operations. Moreover, we cannot predict the size of future issuances of our common stock, as well as securities convertible into or exercisable for common stock, or the effect, if any, that future issuances and sales of our securities will have on the market price of our common stock. Sales of substantial amounts of our common stock, as well as securities convertible into or exercisable for common stock, including shares issued in connection with an acquisition or securing funds to complete any clinical trial plans, or the perception that such sales could occur, may result in substantial dilution and may adversely affect prevailing market prices for our common stock.

We plan to sell shares of our common stock in “at-the-market offerings”, and investors who buy shares of our common stock at different times will likely pay different prices.

Investors who purchase shares of our common stock in the offering described in this prospectus supplement at different times will likely pay different prices and may experience different outcomes in their investment results. We will have discretion, subject to the effect of market conditions, to vary the timing, prices, and numbers of shares sold in this offering. Investors may experience a decline in the value of their shares of our common stock. The trading price of our common stock may be volatile and subject to wide fluctuations.

We have never paid dividends on our capital stock and we do not anticipate paying dividends in the foreseeable future.

We have never paid dividends on any of our capital stock and currently intend to retain any future earnings to fund the growth of our business. Any determination to pay dividends in the future will be at the discretion of our board of directors and will depend on our financial condition, operating results, capital requirements, general business conditions and other factors that our board of directors may deem relevant. As a result, capital appreciation, if any, of our common stock will be the sole source of gain for the foreseeable future.

The sale or issuance of our common stock to Lincoln Park may cause dilution and the sale of the shares of common stock acquired by Lincoln Park, or the perception that such sales may occur, could cause the price of our common stock to fall.

On September 30, 2020, we entered into a purchase agreement (the Purchase Agreement”) with Lincoln Park Capital Fund, LLC (“Lincoln Park”), pursuant to which Lincoln Park has committed to purchase up to \$25.0 million of our common stock, subject to certain limitations. Upon the execution of the Purchase Agreement, we issued 180,701 Commitment Shares to Lincoln Park in consideration for its commitment to purchase additional shares of our common stock under the Purchase Agreement. During the year ended December 31, 2020, we issued and sold 353,113 shares, excluding 180,701 shares issued as commitment fee, under the Purchase Agreement for net proceeds of approximately \$0.7 million. From January 1, 2021 through the date of this prospectus supplement, we issued and sold 985,186 shares of our common stock under the Purchase Agreement for net proceeds of \$2.9 million. The remaining shares of our common stock that may be issued under the Purchase Agreement may be sold by us to Lincoln Park at our discretion from time to time over a 36-month period commencing after the satisfaction of certain conditions set forth in the Purchase Agreement. The purchase price for the shares that we may sell to Lincoln Park under the Purchase Agreement will fluctuate based on the price of our common stock. Depending on market liquidity at the time, sales of such shares may cause the trading price of our common stock to fall.

We generally have the right to control the timing and amount of any future sales of our shares to Lincoln Park. Additional sales of our common stock, if any, to Lincoln Park will depend upon market conditions and other factors to be determined by us. We may ultimately decide to sell to Lincoln Park all, some, or none of the additional shares of our common stock that may be available for us to sell pursuant to the Purchase Agreement. If and when we do sell shares to Lincoln Park, after Lincoln Park has acquired the shares, Lincoln Park may resell all or some of those shares at any time or from time to time in its discretion. Therefore, sales to Lincoln Park by us could result in substantial dilution to the interests of other holders of our common stock. Additionally, the sale of a substantial number of shares of our common stock to Lincoln Park, or the anticipation of such sales, could make it more difficult for us to sell equity or equity-related securities in the future at a time and at a price that we might otherwise wish to effect sales.

FORWARD-LOOKING STATEMENTS

This prospectus supplement and the documents incorporated herein by reference contain forward-looking statements which are made pursuant to the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Statements other than statements of historical fact constitute “forward-looking statements.” These forward-looking statements do not constitute guarantees of future performance. These forward-looking statements may be identified by terms such as “intend,” “expect,” “believe,” “anticipate,” “will,” “should,” “would,” “could,” “may,” “designed,” “potential,” “evaluate,” “progressing,” “proceeding,” “exploring,” “hopes,” and similar expressions, or the negative of such expressions. Such statements are based upon certain assumptions and assessments made by our management in light of their experience and their perception of historical trends, current conditions, expected future developments and other factors they believe to be appropriate.

These statements include, without limitation, statements regarding: our anticipated expenditures, including research and development, sales and marketing, and general and administrative expenses; our ability to benefit from the NIH/NCI award for continued clinical development of RNL™ for recurrent glioblastoma; the ability of RNL™ to safely and effectively deliver radiation directly to the tumor at large doses; the duration of any therapies employing RNL™; our ability to expand testing of RNL™ to additional sites; the potential size of the market for our product candidates; future development and/or expansion of our product candidates and therapies in our markets; our ability to generate product or development revenues and the sources of such revenue; the amounts that we will be obligated to pay under license agreements; our ability to effectively manage our gross profit margins; our ability to obtain and maintain regulatory approvals; expectations as to our future performance; portions of the “Liquidity and Capital Resources” section of our annual and quarterly reports filed with the SEC; our ability to fully access our equity line with Lincoln Park; our need for additional financing and the availability thereof; any changes to our interest expenses; our ability to continue as a going concern; our ability to remain listed on the Nasdaq Capital Market; our ability to repay or refinance some or all of our outstanding indebtedness and our ability to raise capital in the future; our expectations as to the impact of recently issued or adopted accounting standards; our expectations as to the impact of the COVID-19 pandemic on our business and operating results; our beliefs as to the impact of any liability that may arise as a result of any legal proceedings; and the potential enhancement of our cash position through development, marketing, and licensing arrangements.

Our actual results may differ, including materially, from those anticipated in these forward-looking statements as a result of various risks and uncertainties. These risks and uncertainties include, but are not limited to, those risks discussed in “Risk Factors,” the risks described under “Part I—Item 1A—Risk Factors” in our Annual Report on Form 10-K for the year ended December 31, 2020, and under “Part II, Item 1A—Risk Factors” in our Quarterly Reports on Form 10-Q incorporated herein by reference, as well as, without limitation, risks associated with:

- uncertainties relating to the clinical trials of our product candidates and therapies;
- the outcome of our partnering/licensing efforts;
- risks associated with laws or regulatory requirements applicable to us;
- the strategies, prospects, plans, expectations and objectives of management for future operations, including the anticipated timing of regulatory submissions or actions;
- public health crises, pandemics and epidemics, such as the novel strain of coronavirus (COVID-19), and their effects on our preclinical and planned clinical activities;
- our need and ability to raise additional capital to continue our development programs;

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- market conditions;
 - the progress, scope or duration of the development of product candidates or programs;
 - the benefits that may be derived from product candidates or the commercial or market opportunity in any target indication;
 - our ability to protect our intellectual property rights;
 - our anticipated operations, financial position, costs or expenses;
 - statements regarding future economic conditions or performance;
 - statements concerning proposed new products, services or developments;
 - statements of belief and any statement of assumptions underlying any of the foregoing;
 - our ability to sell shares of common stock to Lincoln Park pursuant to the terms of the Purchase Agreement and our ability to register and maintain the registration of the shares issued and issuable thereunder; and
 - our anticipated use of the net proceeds from the potential sale of shares of our common stock in this offering.

We encourage you to read these risks carefully. We caution you not to place undue reliance on the forward-looking statements contained in this prospectus supplement. These forward-looking statements speak only as of the date made. We assume no obligation or undertaking to update any forward-looking statements to reflect any changes in expectations with regard thereto or any change in events, conditions or circumstances on which any such statement is based. You should, however, review additional disclosures we make in the reports we file with the Securities and Exchange Commission (“SEC”).

USE OF PROCEEDS

We may issue and sell shares of common stock having aggregate sales proceeds of up to \$5,040,000 from time to time in this offering. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and net proceeds to us, if any, are not determinable at this time. There can be no assurance that, in the future, we will sell any shares under or fully utilize the sales agreement with Canaccord as a source of financing.

We intend to use the net proceeds from this offering for general corporate purposes and working capital. We may also use a portion of the net proceeds from this offering to acquire or invest in complementary businesses, technologies, product candidates or other intellectual property, although we have no present commitments or agreements to do so.

The amounts and timing of these expenditures will depend on a number of factors, such as the timing and progress of our research and development efforts, regulatory actions affecting our product candidates and our business, technological advances and the competitive environment for our product candidates. As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses for the net proceeds to us from this offering. Accordingly, we will retain broad discretion over the use of these proceeds. Pending use of the net proceeds as described above, we expect to invest the net proceeds in short- and intermediate-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government.

DILUTION

If you purchase our common stock in this offering, your ownership interest will be immediately diluted to the extent of the difference between the public offering price per share and the net tangible book value per share of our common stock immediately after this offering. Net tangible book value per share is determined by dividing the number of shares of common stock outstanding as of December 31, 2020 into our total tangible assets less total liabilities.

Our net tangible book value as of December 31, 2020 was \$2,573,000, or \$0.38 per share, based on 6,749,028 shares of our common stock outstanding as of that date. After giving effect to the sale of 1,396,122 shares of common stock by us at an assumed public offering price of \$3.61 per share, the last reported sale price of our common stock on the Nasdaq Capital Market on February 19, 2021, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of December 31, 2020 would have been approximately \$7.3 million, or approximately \$0.90 per share. This represents an immediate increase in net tangible book value of approximately \$0.52 per share to existing stockholders and immediate dilution of approximately \$2.71 per share to investors purchasing shares of common stock in this offering, as illustrated by the following table:

Assumed public offering price per share	<u>\$ 3.61</u>
Net tangible book value per share as of December 31, 2020	<u>\$0.38</u>
Increase in net tangible book value per share attributable to investors participating in this offering	<u>\$0.52</u>
As adjusted net tangible book value per share after giving effect to this offering	<u>(0.90)</u>
Dilution per share to investors in this offering	<u>\$ 2.71</u>

The table above assumes for illustrative purposes that an aggregate of 1,396,122 shares of our common stock are sold at a price of \$3.61 per share, the last reported sale price of our common stock on the Nasdaq Capital Market on February 19, 2021, for aggregate gross proceeds of \$5,040,000. The shares sold in this offering, if any, will be sold from time to time at various prices. A \$1.00 increase in the price at which the shares are sold from the assumed public offering price of \$3.61 per share, would increase our as adjusted net tangible book value by approximately \$0.04 per share, and the dilution per share to investors in this offering by approximately \$0.97 per share, after deducting estimated commissions and estimated offering expenses payable by us. A \$1.00 decrease in the price at which the shares are sold from the assumed public offering price of \$3.61 per share, would decrease our as adjusted net tangible book value by approximately \$0.06 per share, and the dilution per share to investors in this offering by approximately \$0.94 per share, after deducting estimated commissions and estimated offering expenses payable by us. The as adjusted information provided above is illustrative only. The common stock sold in this offering, if any, will be sold from time to time at various prices.

The number of shares of common stock to be outstanding immediately after this offering in the table above is based on 6,749,028 shares outstanding as of December 31, 2020 and excludes:

- 531,336 shares of common stock issuable upon exercise of stock options outstanding as of December 31, 2020 under our equity incentive plans, with a weighted-average exercise price of \$10.01 per share;
- 159,939 shares of common stock reserved for future issuance under our 2020 Stock Incentive Plan;
- 210,389 shares of common stock reserved for future issuance under our 2015 New Employee Incentive Plan;

- 6,096 and 416,889 shares of common stock issuable upon conversion of 1,016 shares of Series B Convertible Preferred Stock and 938 shares of Series C Preferred Stock, respectively, outstanding as of December 31, 2020; and
- 3,113,625 shares of common stock issuable upon the exercise of warrants to purchase common stock outstanding as of December 31, 2020, with a weighted-average exercise price of \$2.62 per share.

To the extent that additional shares are issued pursuant to the foregoing, investors purchasing our common stock in this offering will experience further dilution. In addition, we may offer other securities in other offerings due to market conditions or strategic considerations. To the extent we issue such securities, investors may experience further dilution.

PLAN OF DISTRIBUTION

We have entered into a sales agreement with Canaccord Genuity LLC, or Canaccord, under which we may issue and sell shares of our common stock from time to time through or to Canaccord acting as sales agent or principal, subject to certain limitations, having an aggregate gross sales price of up to \$10,000,000. We previously sold \$4,958,189 in shares of our common stock pursuant to a prior prospectus supplement, which offered up to \$4,960,000 in shares of our common stock. This prospectus supplement is offering \$5,040,000 in shares of our common stock. Sales of our common stock, if any, under this prospectus supplement and the accompanying prospectus may be made in sales deemed to be “at the market offerings” as defined in Rule 415 promulgated under the Securities Act. We may instruct Canaccord not to sell our common stock if the sales cannot be effected at or above the price designated by us from time to time. We or Canaccord may suspend the offering of our common stock upon notice and subject to other conditions. As our agent, Canaccord will not engage in any transactions that stabilize the price of our common stock.

Each time we wish to issue and sell common stock under the sales agreement, we will notify Canaccord of the number or dollar value of shares to be sold, the dates on which such sales are anticipated to be made, any minimum price below which sales may not be made and other sales parameters as we deem appropriate. Once we have so instructed Canaccord, unless Canaccord declines to accept the terms of the notice, Canaccord has agreed to use its commercially reasonable efforts consistent with its normal trading and sales practices to sell such shares up to the amount specified on such terms. The obligation of Canaccord under the sales agreement to sell shares of our common stock is subject to a number of conditions that we must meet.

We will pay Canaccord a commission equal to 3.0% of the gross proceeds we receive from the sales of our common stock under the sales agreement. Because there is no minimum offering amount required as a condition to closing this offering, the actual total public offering amount, Canaccord’s commission and proceeds to us, if any, are not determinable at this time. In addition, we have agreed to reimburse Canaccord for its reasonable documented out-of-pocket expenses, including fees and disbursements of its counsel, in the amount of \$50,000. We estimate that the total expenses of the offering payable by us, excluding commissions payable to Canaccord under the sales agreement, will be approximately \$100,000.

Settlement for sales of our common stock will occur on the second trading day following the date on which any sales are made, in return for payment of the net proceeds to us. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

In connection with the sale of the common stock on our behalf, Canaccord will be deemed to be an “underwriter” within the meaning of the Securities Act, and the compensation of Canaccord will be deemed to be underwriting commission or discount. We have agreed to provide indemnification and contribution to Canaccord against certain liabilities, including liabilities under the Securities Act.

The offering pursuant to the sales agreement will terminate upon the earlier of (i) the issuance and sale of all shares of our common stock subject to the sales agreement, or (ii) the termination of the sales agreement as permitted therein.

Canaccord and its affiliates may in the future provide various investment banking and other financial services for us and our affiliates, for which services they may in the future receive customary fees. To the extent required by Regulation M, Canaccord will not engage in any market making activities involving our common stock while the offering is ongoing under this prospectus supplement.

LEGAL MATTERS

The validity of the common stock offered by this prospectus supplement will be passed upon for us by Pillsbury Winthrop Shaw Pittman LLP, Palo Alto, California. Canaccord Genuity LLC is being represented by Goodwin Procter LLP, New York, New York, in connection with this offering.

EXPERTS

The consolidated financial statements as of December 31, 2020 and 2019 and for the years then ended incorporated by reference in this prospectus supplement have been so incorporated in reliance on the report of BDO USA, LLP, an independent registered public accounting firm (the report on the consolidated financial statements contains an explanatory paragraph regarding the Company's ability to continue as a going concern), incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We have filed a registration statement on [Form S-3](#) with the SEC under the Securities Act of 1933. This prospectus supplement and the accompanying prospectus is part of the registration statement but the registration statement includes and incorporates by reference additional information and exhibits. We file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC maintains a web site that contains reports, proxy and information statements and other information regarding companies, such as ours, that file documents electronically with the SEC. The address of that site on the worldwide web is <http://www.sec.gov>.

INCORPORATION BY REFERENCE

The SEC permits us to “incorporate by reference” the information contained in documents we file with the SEC, which means that we can disclose important information to you by referring you to those documents rather than by including them in this prospectus supplement and the accompanying prospectus. Information that is incorporated by reference is considered to be part of this prospectus supplement and the accompanying prospectus and you should read it with the same care that you read this prospectus supplement and the accompanying prospectus. Later information that we file with the SEC will automatically update and supersede the information that is either contained, or incorporated by reference, in this prospectus supplement and the accompanying prospectus, and will be considered to be a part of this prospectus supplement and the accompanying prospectus from the date those documents are filed. We have filed with the SEC, and incorporate by reference in this prospectus supplement and the accompanying prospectus:

- our Annual Report on [Form 10-K](#) for the year ended December 31, 2020 (filed with the SEC on February 22, 2021);
- our Current Reports on Form 8-K filed with the SEC on [January 12, 2021](#) and [February 23, 2021](#) (in each case, to the extent filed and not furnished); and
- the description of our common stock contained in our Registration Statement on [Form 10/A](#) filed on July 16, 2001, and any amendment or report filed with the Commission for the purpose of updating the description.

We also incorporate by reference all additional documents that we file with the SEC under the terms of Section 13(a), 13(c), 14 or 15(d) of the Exchange Act that are made after the initial filing date of the registration statement of which this prospectus is a part and the effectiveness of the registration statement, as well as between the date of this prospectus and the termination of any offering of securities offered by this prospectus (excluding any portions thereof furnished by the Registrant, including but not limited to information furnished under Item 2.02 and Item 7.01 and any exhibits relating to Item 2.02 or Item 7.01 furnished under Item 9.01 of Form 8-K and any certification required by 18 U.S.C. § 1350).

Any statement contained in this Registration Statement or in a document incorporated by reference in this Registration Statement shall be deemed to be modified or superseded for purposes of this Registration Statement to the extent that a statement contained in this Registration Statement or in any subsequently filed document that is deemed to be incorporated by reference in this Registration Statement modifies or supersedes such statement.

We make available free of charge on our website our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports, as soon as reasonably practicable after we electronically file or furnish such materials to the Securities and Exchange Commission, or SEC. You may obtain a free copy of these reports in the Investor Relations section of our website, www.plustherapeutics.com. The contents of our website are not part of this prospectus supplement and the references in this prospectus supplement, the accompanying prospectus and the documents we have incorporated by reference to our website do not constitute incorporation by reference into this prospectus supplement or the accompanying prospectus of the information contained therein.

\$100,000,000



Plus Therapeutics, Inc.

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

We may, from time to time, offer and sell the securities identified above in one or more offerings. The aggregate initial offering price of all securities sold under this prospectus will not exceed \$100,000,000.

This prospectus describes the general terms of these securities and the general manner in which these securities will be offered. We will provide the specific terms of these securities in supplements to this prospectus. The prospectus supplements will also describe the manner in which these securities will be offered and may also add to, update or change information contained in this prospectus. You should read carefully this prospectus and the accompanying prospectus supplement before you invest.

We may offer and sell the securities separately or together in any combination for sale directly to investors or through underwriters, dealers or agents. If any underwriters, dealers or agents are involved in the sale of these securities we will set forth their names and describe their compensation in the applicable prospectus supplement.

Our common stock is listed on the Nasdaq Capital Market under the symbol "PSTV." On October 7, 2020, the last reported sale price of our common stock on the Nasdaq Capital Market was \$2.55 per share.

Investing in our securities involves risks. See the section entitled "Risk Factors" included in or incorporated by reference into the accompanying prospectus supplement and in the documents we incorporate by reference in this prospectus.

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

The date of this prospectus is October 19, 2020

TABLE OF CONTENTS

	Page
<u>ABOUT THIS PROSPECTUS</u>	1
<u>RISK FACTORS</u>	1
<u>PLUS THERAPEUTICS, INC.</u>	1
<u>FORWARD-LOOKING STATEMENTS</u>	2
<u>USE OF PROCEEDS</u>	2
<u>DESCRIPTION OF DEBT SECURITIES</u>	3
<u>DESCRIPTION OF CAPITAL STOCK</u>	9
<u>DESCRIPTION OF DEPOSITARY SHARES</u>	13
<u>DESCRIPTION OF WARRANTS</u>	16
<u>DESCRIPTION OF RIGHTS</u>	16
<u>FORMS OF SECURITIES</u>	17
<u>PLAN OF DISTRIBUTION</u>	19
<u>LEGAL MATTERS</u>	20
<u>EXPERTS</u>	20
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	21
<u>INCORPORATION BY REFERENCE</u>	21

You should rely only on the information incorporated by reference or provided in this prospectus, any prospectus supplement, any applicable free writing prospectus and the registration statement. We have not authorized anyone else to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information in this prospectus, any prospectus supplement, any applicable free writing prospectus or the documents incorporated by reference, is accurate only as of the dates of those documents. Our business, financial condition, results of operations and prospects may have changed since those dates.

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, using a “shelf” registration, or continuous offering, process. Under this shelf registration process, we may, from time to time, offer and sell separately or together in any combination the securities described in this prospectus in one or more offerings up to a maximum aggregate offering price of \$100,000,000.

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide a prospectus supplement that will contain specific information about the terms of that offering and the offered securities. Any prospectus supplement, or information incorporated by reference in this prospectus or any prospectus supplement that is of a more recent date, may also add, update or change information contained in this prospectus. Any statement that we make in this prospectus will be modified or superseded by any inconsistent statement made by us in a prospectus supplement. The registration statement we filed with the SEC includes exhibits that provide more detail of the matters discussed in this prospectus. You should read this prospectus and the related exhibits filed with the SEC, any prospectus supplement, and any applicable free writing prospectus, together with additional information described under the headings “Where You Can Find More Information,” and “Incorporation by Reference,” before making your investment decision.

All references in this prospectus supplement to “Plus,” the “company,” “we,” “us” and “our” refer to Plus Therapeutics, Inc. and its consolidated subsidiaries, except where the context otherwise requires or as otherwise indicated.

“Plus Therapeutics,” “PSTV” and the Plus logo are our trademarks. This prospectus and the documents incorporated by reference into this prospectus may also contain trademarks and trade names that are the property of their respective owners. We do not intend our use or display of other companies’ trade names, trademarks or service marks to imply relationships with, or endorsements or sponsorship of us by, these other companies.

RISK FACTORS

Investing in our securities involves risk. The prospectus supplement relating to a particular offering will contain or incorporate by reference a discussion of risks applicable to an investment in the securities offered. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed under the heading “Risk Factors” included in or incorporated by reference into the applicable prospectus supplement together with all of the other information contained in the prospectus supplement or appearing in or incorporated by reference into this prospectus, including the risk factors incorporated by reference to our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q or Current Reports on Form 8-K. The occurrence of any of these risks might cause you to lose all or part of your investment in the offered securities.

PLUS THERAPEUTICS, INC.

We are a clinical-stage pharmaceutical company focused on the discovery, development, and manufacturing scale up of complex and innovative treatments for patients battling cancer and other life-threatening diseases. Our proprietary nanotechnology platform is currently centered around the enhanced delivery of a variety of drugs using novel liposomal encapsulation technology. Liposomal encapsulation has been extensively explored and undergone significant technical and commercial advances since it was first developed. Our platform is designed to facilitate new delivery approaches and/or formulations of safe and effective, injectable drugs, potentially enhancing the safety, efficacy and convenience for patients and healthcare providers.

We plan to leverage our nanotechnology platform and expertise using a simple multi-step model that enables us to address unmet needs or underserved conditions while managing risks and minimizing development costs through: (1) mapping of the current and anticipated market landscape to clearly understand the clinical and commercial opportunities and defining nanotechnology options, (2) redesign of known, safe and effective active pharmaceutical ingredients with new nanotechnology, (3) manufacture-to-scale of the reformulated drug along with critical non-clinical (i.e., bench, animal) analyses, (4) evaluation of early-stage clinical utility with a focus on proving safety and defining efficacy over the current standard of care, and (5) partnering the innovative treatment for late-stage clinical trials, regulatory approval, and commercial launch.

We were initially formed as a California general partnership in July 1996 and incorporated in the State of Delaware in May 1997. We were formerly known as Cytori Therapeutics, Inc., before that as MacroPore Biosurgery, Inc. and before that as MacroPore, Inc. Our corporate offices are located at 4200 Marathon Blvd., Suite 200, Austin, Texas 78756. Our telephone number is (737) 255-7194. We maintain a website at www.plustherapeutics.com. The information found on our website, or that may be accessed by links on our website, is not part of this prospectus. We have included our website address solely as an inactive textual reference. Investors should not rely on any such information in deciding whether to purchase our common stock.

FORWARD-LOOKING STATEMENTS

When used in this prospectus, words such as “*intend*,” “*expect*,” “*believe*,” “*anticipate*,” “*will*,” “*should*,” “*would*,” “*could*,” “*may*,” “*designed*,” “*potential*,” and similar expressions, or the negative of such expressions, are intended to identify forward-looking statements. These statements are subject to known and unknown risks and uncertainties that could cause actual results to differ materially from those projected or otherwise implied by the forward-looking statements. These forward-looking statements speak only as of the date of this prospectus. Given these risks and uncertainties, you should not place undue reliance on these forward-looking statements. We will discuss many of these risks and uncertainties in greater detail in any prospectus supplement under the heading “Risk Factors.” Additional cautionary statements or discussions of risks and uncertainties that could affect our results or the achievement of the expectations described in forward-looking statements may also be contained in the documents we incorporate by reference into this prospectus.

These forward-looking statements speak only as of the date of this prospectus. We expressly disclaim any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in our expectations with regard thereto or any change in events, conditions or circumstances on which any such statement is based. You should, however, review additional disclosures we make in our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, and Current Reports on Form 8-K filed with the SEC.

USE OF PROCEEDS

Unless we state otherwise in the applicable prospectus supplement, we intend to use the net proceeds from the sale of the securities offered by this prospectus for general corporate purposes. General corporate purposes may include additions to working capital, financing of capital expenditures, repayment or redemption of existing indebtedness, repurchases of stock and future acquisitions and strategic investment opportunities. Unless we state otherwise in the applicable prospectus supplement, pending the application of net proceeds, we expect to invest the net proceeds in short- and intermediate-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government.

DESCRIPTION OF DEBT SECURITIES

The following is a summary of the general terms of the debt securities. We will file a prospectus supplement that may contain additional terms when we issue debt securities. The terms presented here, together with the terms in a related prospectus supplement, together with any pricing supplement or term sheet, will be a description of the material terms of the debt securities.

We may issue, from time to time, debt securities, in one or more series. These debt securities that we may issue include senior debt securities, senior subordinated debt securities, subordinated debt securities, convertible debt securities and exchangeable debt securities. The debt securities we offer will be issued under an indenture between us and the trustee named in the indenture. The following is a summary of the material provisions of the form of indenture filed as an exhibit to the registration statement of which this prospectus is a part. All capitalized terms have the meanings specified in the indentures. For each series of debt securities, the applicable prospectus supplement for the series may change and supplement the summary below.

As used in this section only, “we,” “us” and “our” refer to Plus Therapeutics, Inc. excluding any subsidiaries, unless expressly stated or the context otherwise requires.

General Terms of the Indenture

The indenture does not limit the amount of debt securities that we may issue. It provides that we may issue debt securities for any series of debt securities up to the principal amount that we may authorize. Except for the limitations on consolidation, merger and sale of all or substantially all of our assets contained in the indenture, the terms of the indenture do not contain any covenants or other provisions designed to give holders of any debt securities protection against changes in our operations, financial condition or transactions involving us. For each series of debt securities, any restrictive covenants for those debt securities will be described in the applicable prospectus supplement for those debt securities.

We may issue the debt securities issued under the indenture as “discount securities,” which means they may be sold at a discount below their stated principal amount. These debt securities, as well as other debt securities that are not issued at a discount, may, for United States federal income tax purposes, be treated as if they were issued with “original issue discount,” or OID, because of interest payment and other characteristics. Special United States federal income tax considerations applicable to debt securities issued with original issue discount will be described in more detail in any applicable prospectus supplement.

You should refer to the prospectus supplement relating to a particular series of debt securities for a description of the following terms of the debt securities offered by that prospectus supplement and by this prospectus:

- the title of those debt securities;
- any limit on the aggregate principal amount of that series of debt securities;
- the date or dates on which principal and premium, if any, of the debt securities of that series is payable;
- the interest rate or rates (which may be fixed or variable) or the method or methods used to determine the rate or rates, and the date or dates from which interest, if any, on the debt securities of that series will accrue, and the dates when interest is payable and related record dates, and the maturity;
- the right, if any, to extend the interest payment periods and the duration of the extensions;
- if the amount of payments of principal or interest is to be determined by reference to an index or formula, or based on a coin or currency other than that in which the debt securities are stated to be payable, the manner in which these amounts are determined and the calculation agent, if any, with respect thereto;

- the place or places where and the manner in which principal of, premium, if any, and interest, if any, on the debt securities of that series will be payable and the place or places where those debt securities may be presented for transfer and, if applicable, conversion or exchange;
- the period or periods within which, the price or prices at which, and other terms and conditions upon which those debt securities may be redeemed, in whole or in part, at our option or the option of a holder of those securities, if we or a holder is to have that option;
- our obligation or right, if any, to redeem, repay or purchase those debt securities pursuant to any sinking fund or analogous provision or at the option of a holder of those securities, and the terms and conditions upon which the debt securities will be redeemed, repaid or purchased, in whole or in part, pursuant to that obligation;
- the terms, if any, on which the debt securities of that series will be subordinate in right and priority of payment to our other debt;
- the denominations in which those debt securities will be issuable;
- if other than the entire principal amount of the debt securities when issued, the portion of the principal amount payable upon acceleration of maturity as a result of a default on our obligations;
- whether any securities of that series are to be issued in whole or in part in the form of one or more global securities and the depositary for those global securities;
- if the principal of or any premium or interest on the debt securities of that series is to be payable, or is to be payable at our election or the election of a holder of those securities, in securities or other property, the type and amount of those securities or other property, or the manner of determining that amount, and the period or periods within which, and the terms and conditions upon which, any such election may be made;
- the events of default and covenants relating to the debt securities that are in addition to, modify or delete those described in this prospectus;
- conversion or exchange provisions, if any, including conversion or exchange prices or rates and adjustments thereto;
- whether and upon what terms the debt securities may be defeased, if different from the provisions set forth in the indenture;
- the nature and terms of any security for any secured debt securities;
- the terms applicable to any debt securities issued at a discount from their stated principal amount; and
- any other specific terms of any debt securities.

The applicable prospectus supplement will present material United States federal income tax considerations for holders of any debt securities and the securities exchange or quotation system on which any debt securities are to be listed or quoted.

Conversion or Exchange Rights

Debt securities may be convertible into or exchangeable for shares of our equity securities or other securities. The terms and conditions of conversion or exchange will be stated in the applicable prospectus supplement. The terms will include, among others, the following:

- the conversion or exchange price;
- the conversion or exchange period;
- provisions regarding our ability or the ability of any holder to convert or exchange the debt securities;

- events requiring adjustment to the conversion or exchange price; and
- provisions affecting conversion or exchange in the event of our redemption of the debt securities.

Consolidation, Merger or Sale

We cannot consolidate with or merge with or into, or transfer or lease all or substantially all of our assets to, any person, unless we are the surviving corporation or the successor person is a corporation organized under the laws of the United States, any state of the United States or the District of Columbia and expressly assumes our obligations under the debt securities and the indenture. In addition, we cannot complete such a transaction unless immediately after completing the transaction, no event of default under the indenture, and no event that, after notice or lapse of time or both, would become an event of default under the indenture, has occurred and is continuing. When the successor person has assumed our obligations under the debt securities and the indenture, we will be discharged from all our obligations under the debt securities and the indenture except in limited circumstances.

This covenant would not apply to any recapitalization transaction, a change of control affecting us or a highly leveraged transaction, unless the transaction or change of control were structured to include a merger or consolidation or transfer or lease of all or substantially all of our assets.

Events of Default

The indenture provides that the following will be “events of default” with respect to any series of debt securities:

- failure to pay interest for 30 days after the date payment is due and payable;
- failure to pay principal or premium, if any, on any debt security when due, either at maturity, upon any redemption, by declaration or otherwise and, in the case of technical or administrative difficulties, only if such default persists for a period of more than three business days;
- failure to make sinking fund payments when due and continuance of such default for a period of 30 days;
- failure to perform other covenants for 60 days after notice that performance was required;
- certain events in bankruptcy, insolvency or reorganization relating to us; or
- any other event of default provided in the applicable officer’s certificate, resolution of our board of directors or the supplemental indenture under which we issue a series of debt securities.

An event of default for a particular series of debt securities does not necessarily constitute an event of default for any other series of debt securities issued under the indenture. For each series of debt securities, any modifications to the above events of default will be described in the applicable prospectus supplement for those debt securities.

The indenture provides that if an event of default specified in the first, second, third, fourth or sixth bullets above occurs and is continuing, either the trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series may declare the principal amount of all those debt securities (or, in the case of discount securities or indexed securities, that portion of the principal amount as may be specified in the terms of that series) to be due and payable immediately. If an event of default specified in the fifth bullet above occurs and is continuing, then the principal amount of all those debt securities (or, in the case of discount securities or indexed securities, that portion of the principal amount as may be specified in the terms of that series) will be due and payable immediately, without any declaration or other act on the part of the trustee or any holder. In certain cases, holders of a majority in principal amount of the outstanding debt securities of any series may, on behalf of holders of all those debt securities, rescind and annul a declaration of acceleration.

The indenture imposes limitations on suits brought by holders of debt securities against us. Except for actions for payment of overdue principal or interest, no holder of debt securities of any series may institute any action against us under the indenture unless:

- the holder has previously given to the trustee written notice of default and continuance of such default;
- the holders of at least 25% in principal amount of the outstanding debt securities of the affected series have requested that the trustee institute the action;
- the requesting holders have offered the trustee indemnity for the reasonable expenses and liabilities that may be incurred by bringing the action;
- the trustee has not instituted the action within 60 days of the request and offer of indemnity; and
- the trustee has not received inconsistent direction by the holders of a majority in principal amount of the outstanding debt securities of the affected series.

We will be required to file annually with the trustee a certificate, signed by one of our officers, stating whether or not the officer knows of any default by us in the performance, observance or fulfillment of any condition or covenant of the indenture.

Discharge, Defeasance and Covenant Defeasance

We can discharge or decrease our obligations under the indenture as stated below.

We may discharge obligations to holders of any series of debt securities that have not already been delivered to the trustee for cancellation and that have either become due and payable or are by their terms to become due and payable, or are scheduled for redemption, within one year. We may effect a discharge by irrevocably depositing with the trustee cash or government obligations, as trust funds, in an amount certified to be enough to pay when due, whether at maturity, upon redemption or otherwise, the principal of, and any premium and interest on, the debt securities and any mandatory sinking fund payments.

Unless otherwise provided in the applicable prospectus supplement, we may also discharge any and all of our obligations to holders of any series of debt securities at any time, which we refer to as defeasance. We may also be released from the obligations imposed by any covenants of any outstanding series of debt securities and provisions of the indenture, and we may omit to comply with those covenants without creating an event of default under the trust declaration, which we refer to as covenant defeasance. We may effect defeasance and covenant defeasance only if, among other things:

- we irrevocably deposit with the trustee cash or government obligations denominated in the currency of the debt securities, as trust funds, in an amount certified to be enough to pay at maturity, or upon redemption, the principal (including any mandatory sinking fund payments) of, and any premium and interest on, all outstanding debt securities of the series; and
- we deliver to the trustee an opinion of counsel from a nationally recognized law firm to the effect that the holders of the series of debt securities will not recognize income, gain or loss for U.S. federal income tax purposes as a result of the defeasance or covenant defeasance and that defeasance or covenant defeasance will not otherwise alter the holders' U.S. federal income tax treatment of principal, and any premium and interest payments on, the series of debt securities.

In the case of a defeasance by us, the opinion we deliver must be based on a ruling of the Internal Revenue Service issued, or a change in U.S. federal income tax law occurring, after the date of the indenture, since such a result would not occur under the U.S. federal income tax laws in effect on that date.

Although we may discharge or decrease our obligations under the indenture as described in the two preceding paragraphs, we may not avoid, among other things, our duty to register the transfer or exchange of any series of debt securities, to replace any temporary, mutilated, destroyed, lost or stolen series of debt securities or to maintain an office or agency in respect of any series of debt securities.

Modification of the Indenture

The indenture provides that we and the trustee may enter into supplemental indentures without the consent of the holders of debt securities to, among other things:

- evidence the assumption by a successor entity of our obligations;
- add to our covenants for the benefit of the holders of debt securities, or to surrender any rights or power conferred upon us;
- add any additional events of default;
- add to, change or eliminate any of the provisions of the indenture in a manner that will become effective only when there is no outstanding debt security which is entitled to the benefit of the provision as to which the modification would apply;
- add guarantees with respect to or secure any debt securities;
- establish the forms or terms of debt securities of any series;
- evidence and provide for the acceptance of appointment by a successor trustee and add to or change any of the provisions of the indenture as is necessary for the administration of the trusts by more than one trustee;
- cure any ambiguity or correct any inconsistency or defect in the indenture;
- modify, eliminate or add to the provisions of the indenture as shall be necessary to effect the qualification of the indenture under the Trust Indenture Act of 1939 or under any similar federal statute later enacted, and to add to the indenture such other provisions as may be expressly required by the Trust Indenture Act; and
- make any other provisions with respect to matters or questions arising under the indenture that will not be inconsistent with any provision of the indenture as long as the new provisions do not adversely affect the interests of the holders of any outstanding debt securities of any series created prior to the modification.

The indenture also provides that we and the trustee may, with the consent of the holders of not less than a majority in aggregate principal amount of debt securities of each series of debt securities affected by such supplemental indenture then outstanding, add any provisions to, or change in any manner, eliminate or modify in any way the provisions of, the indenture or any supplemental indenture or modify in any manner the rights of the holders of the debt securities. We and the trustee may not, however, without the consent of the holder of each outstanding debt security affected thereby:

- extend the final maturity of any debt security;
- reduce the principal amount or premium, if any;
- reduce the rate or extend the time of payment of interest;
- reduce the amount of the principal of any debt security issued with an original issue discount that is payable upon acceleration;

- change the currency in which the principal, and any premium or interest, is payable;
- impair the right to institute suit for the enforcement of any payment on any debt security when due;
- if applicable, adversely affect the right of a holder to convert or exchange a debt security; or
- reduce the percentage of holders of debt securities of any series whose consent is required for any modification of the indenture or for waivers of compliance with or defaults under the indenture with respect to debt securities of that series.

The indenture provides that the holders of not less than a majority in aggregate principal amount of the then outstanding debt securities of any series, by notice to the relevant trustee, may on behalf of the holders of the debt securities of that series waive any default and its consequences under the indenture except:

- a default in the payment of, any premium and any interest on, or principal of, any such debt security held by a non-consenting holder; or
- a default in respect of a covenant or provision of the indenture that cannot be modified or amended without the consent of the holder of each outstanding debt security of each series affected.

Concerning the Trustee

The indenture provides that there may be more than one trustee under the indenture, each for one or more series of debt securities. If there are different trustees for different series of debt securities, each trustee will be a trustee of a trust under the indenture separate and apart from the trust administered by any other trustee under that indenture. Except as otherwise indicated in this prospectus or any prospectus supplement, any action permitted to be taken by a trustee may be taken by such trustee only on the one or more series of debt securities for which it is the trustee under the indenture. Any trustee under the indenture may resign or be removed from one or more series of debt securities. All payments of principal of, and any premium and interest on, and all registration, transfer, exchange, authentication and delivery of, the debt securities of a series will be effected by the trustee for that series at an office designated by the trustee in New York, New York.

The indenture provides that, except during the continuance of an event of default, the trustee will perform only such duties as are specifically set forth in the indenture. During the existence of an event of default, the trustee will exercise those rights and powers vested in it under the indenture and use the same degree of care and skill in its exercise as a prudent person would exercise under the circumstances in the conduct of such person's own affairs.

If the trustee becomes a creditor of ours, the indenture places limitations on the right of the trustee to obtain payment of claims or to realize on property received in respect of any such claim as security or otherwise. The trustee may engage in other transactions. If it acquires any conflicting interest relating to any duties concerning the debt securities, however, it must eliminate the conflict or resign as trustee.

No Individual Liability of Incorporators, Stockholders, Officers or Directors

The indenture provides that no past, present or future director, officer, stockholder or employee of ours, any of our affiliates, or any successor corporation, in their capacity as such, shall have any individual liability for any of our obligations, covenants or agreements under the debt securities or the indenture.

Governing Law

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

DESCRIPTION OF CAPITAL STOCK

This section describes the general terms and provisions of the shares of our common stock, par value \$0.001 per share, and preferred stock, par value \$0.001 per share. This description is only a summary. Our amended and restated certificate of incorporation, as amended and our amended and restated bylaws have been filed as exhibits to our periodic reports filed with the SEC, which are incorporated by reference in this prospectus. You should read our amended and restated certificate of incorporation and our amended and restated bylaws for additional information before you buy any of our common stock, preferred stock or other securities. See “Where You Can Find More Information.”

Common Stock

We are authorized to issue 100,000,000 shares of common stock. As of September 30, 2020, there were 4,591,415 shares of common stock issued and outstanding. Each holder of common stock is entitled to one vote for each share of common stock held on all matters submitted to a vote of stockholders. We have not provided for cumulative voting for the election of directors in our amended and restated certificate of incorporation, as amended. This means that the holders of a majority of the shares voted can elect all of the directors then standing for election. Subject to preferences that may apply to shares of preferred stock outstanding at the time, the holders of outstanding shares of our common stock are entitled to receive dividends out of assets legally available at the times and in the amounts that our board of directors may determine from time to time. Upon our liquidation, dissolution or winding-up, the holders of common stock are entitled to share ratably in all assets remaining after payment of all liabilities and the liquidation preferences of any outstanding preferred stock. Holders of common stock have no preemptive or conversion rights or other subscription rights. There are no redemption or sinking fund provisions applicable to the common stock. All outstanding shares of common stock are fully paid and nonassessable.

Preferred Stock

We are authorized to issue 5,000,000 shares of preferred stock, 1,959 shares of which were issued and outstanding as of September 30, 2020. Of this amount, (i) 13,500 shares have been designated Series A 3.6% Convertible Preferred Stock, 0 shares of which are outstanding, (ii) 10,000 shares have been designated Series B Convertible Preferred Stock, 1,016 shares of which are outstanding, and (iii) 7,000 shares have been designated Series C Convertible Preferred Stock, 938 shares of which are outstanding.

We may issue additional shares of preferred stock, in series, with such designations, powers, preferences and other rights and qualifications, limitations or restrictions as our board of directors may authorize, without further action by our stockholders, including:

- the distinctive designation of each series and the number of shares that will constitute the series;
- the voting rights, if any, of shares of the series and the terms and conditions of the voting rights;
- the dividend rate on the shares of the series, the dates on which dividends are payable, any restriction, limitation or condition upon the payment of dividends, whether dividends will be cumulative, and the dates from and after which dividends shall accumulate;
- the prices at which, and the terms and conditions on which, the shares of the series may be redeemed, if the shares are redeemable;
- the terms and conditions of a sinking or purchase fund for the purchase or redemption of shares of the series, if such a fund is provided;
- any preferential amount payable upon shares of the series in the event of the liquidation, dissolution or winding up of, or upon the distribution of any of our assets; and

- the prices or rates of conversion or exchange at which, and the terms and conditions on which, the shares of the series may be converted or exchanged into other securities, if the shares are convertible or exchangeable.

The particular terms of any additional series of preferred stock, and the transfer agent and registrar for that series, will be described in a prospectus supplement. Any material United States federal income tax consequences and other special considerations with respect to any preferred stock offered under this prospectus will also be described in the applicable prospectus supplement.

The issuance of preferred stock could decrease the amount of earnings and assets available for distribution to holders of our common stock or adversely affect the rights and powers, including voting rights, of the holders of our common stock. The issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our company, which could depress the market price of our common stock.

Series B Preferred Stock

Conversion. Each share of Series B Preferred Stock is convertible, at our option or at the option of the holder at any time, into the number of shares of our common stock determined by dividing the \$1,000 stated value per share of the Series B Preferred Stock by a conversion price of \$166.65 per share. In addition, the conversion price per share is subject to adjustment for stock dividends, distributions, subdivisions, combinations or reclassifications. Subject to limited exceptions, a holder of the Series B Preferred Stock will not have the right to convert any portion of the Series B Preferred Stock to the extent that, after giving effect to the conversion, the holder, together with its affiliates, would beneficially own in excess of 9.99% of the number of shares of our common stock outstanding immediately after giving effect to its conversion.

Fundamental Transactions. In the event we effect certain mergers, consolidations, sales of substantially all of our assets, tender or exchange offers, reclassifications or share exchanges in which our common stock is effectively converted into or exchanged for other securities, cash or property, we consummate a business combination in which another person acquires 50% of the outstanding shares of our common stock, or any person or group becomes the beneficial owner of 50% of the aggregate ordinary voting power represented by our issued and outstanding common stock, then, upon any subsequent conversion of the Series B Preferred Stock, a holder of the Series B Preferred Stock will have the right to receive any shares of the acquiring corporation or other consideration it would have been entitled to receive if it had been a holder of the number of shares of common stock then issuable upon conversion in full of the Series B Preferred Stock.

Dividends. Holders of Series B Preferred Stock are entitled to receive dividends (on an as-if-converted-to-common-stock basis) in the same form as dividends actually paid on shares of the common stock when, as and if such dividends are paid on shares of common stock.

Voting Rights. Except as otherwise provided in the certificate of designation for the Series B Preferred Stock or as otherwise required by law, the Series B Preferred Stock has no voting rights.

Liquidation Preference. Upon our liquidation, dissolution or winding-up, whether voluntary or involuntary, holders of Series B Preferred Stock will be entitled to receive out of our assets, whether capital or surplus, an amount equal to the \$1,000 stated value per share for each share of Series B Preferred Stock before any distribution or payment shall be made to the holders of any junior securities.

Redemption Rights. We are not obligated to redeem or repurchase any shares of Series B Preferred Stock. Shares of Series B Preferred Stock are not otherwise entitled to any redemption rights, or mandatory sinking fund or analogous fund provisions.

Series C Preferred Stock

Conversion. Each share of Series C Preferred Stock will be convertible, at our option at any time on or after July 25, 2020, subject to certain conditions, or at the option of the holder at any time, into the number of shares of our common stock determined by dividing the \$1,000 stated value per share of the Series C Preferred Stock by a conversion price of \$2.25. In addition, the conversion price per share is subject to adjustment for stock dividends, distributions, subdivisions, combinations or reclassifications. Subject to limited exceptions, a holder of the Series C Preferred Stock will not have the right to convert any portion of the Series C Preferred Stock to the extent that, after giving effect to the conversion, the holder, together with its affiliates, would beneficially own in excess of 9.99% of the number of shares of our common stock outstanding immediately after giving effect to its conversion.

Anti-Dilution. Subject to certain exceptions contained in the certificate of designation for the Series C Preferred Stock, including our ability to issue securities in connection with equity awards to service providers, strategic transactions, debt financings, research and development partnerships, an equity line of credit, our “at the market” equity offering program and other customary exceptions, if we issue or sell, or are deemed to have issued or sold, any shares of common stock or Common Stock Equivalents (as defined in the certificate of designation) for a consideration per share lower than the conversion price of the Series C Preferred Stock in effect immediately prior to such issuance or sale, or deemed issuance or sale, then the conversion price of the Series C Preferred Stock then in effect will be reduced to an amount equal to such lower price pursuant to the terms of the certificate of designation.

Fundamental Transactions. In the event we effect certain mergers, consolidations, sales of substantially all of our assets, tender or exchange offers, reclassifications or share exchanges in which our common stock is effectively converted into or exchanged for other securities, cash or property, we consummate a business combination in which another person acquires 50% of the outstanding shares of our common stock, or any person or group becomes the beneficial owner of 50% of the aggregate ordinary voting power represented by our issued and outstanding common stock, then, upon any subsequent conversion of the Series C Preferred Stock, a holder of the Series C Preferred Stock will have the right to receive any shares of the acquiring corporation or other consideration it would have been entitled to receive if it had been a holder of the number of shares of common stock then issuable upon conversion in full of the Series C Preferred Stock.

Dividends. Holders of Series C Preferred Stock are entitled to receive dividends (on an as-if-converted-to-common-stock basis) in the same form as dividends actually paid on shares of the common stock when, as and if such dividends are paid on shares of common stock.

Voting Rights. Except as otherwise provided in the certificate of designation for the Series C Preferred Stock or as otherwise required by law, the Series C Preferred Stock has no voting rights.

Liquidation Preference. Upon our liquidation, dissolution or winding-up, whether voluntary or involuntary, holders of Series C Preferred Stock will be entitled to receive out of our assets, whether capital or surplus, an amount equal to the \$1,000 stated value per share for each share of Series C Preferred Stock before any distribution or payment shall be made to the holders of any junior securities.

Redemption Rights. We are not obligated to redeem or repurchase any shares of Series C Preferred Stock. Shares of Series C Preferred Stock are not otherwise entitled to any redemption rights, or mandatory sinking fund or analogous fund provisions.

Anti-Takeover Effects of Delaware Law and Our Certificate of Incorporation and Bylaws

Certain provisions of Delaware law, our amended and restated certificate of incorporation, as amended and our amended and restated bylaws could have the effect of delaying, deferring or discouraging another party from

acquiring control of us. These provisions, which are summarized below, are expected to discourage certain types of coercive takeover practices and inadequate takeover bids. These provisions are also designed, in part, to encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of increased protection of our potential ability to negotiate with an unfriendly or unsolicited acquirer outweigh the disadvantages of discouraging such proposals, including proposals that are priced above the then-current market value of our common stock, because, among other reasons, the negotiation of such proposals could result in an improvement of their terms.

Certificate of Incorporation and Bylaws. Our amended and restated certificate of incorporation, as amended and amended and restated bylaws include provisions that:

- authorize the board of directors to issue, without stockholder approval, blank-check preferred stock with such designations, powers, preferences and other rights and qualifications, limitations or restrictions as our board of directors may authorize, which preferred stock could decrease the amount of earnings and assets available for distribution to holders of our common stock or adversely affect the rights and powers, including voting rights, of the holders of our common stock;
- establish advance notice requirements for stockholder nominations of directors and for stockholder proposals that can be acted on at stockholder meetings;
- limit who may call stockholder meetings;
- require that any action to be taken by our stockholders be effected at a duly called annual or special meeting and not by written consent;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even if less than a quorum; and
- authorize us to indemnify officers and directors against losses that they may incur in investigations and legal proceedings resulting from their services to us, which may include services in connection with takeover defense measures.

Delaware anti-takeover statute. We are subject to the provisions of Section 203 of the General Corporation Law of the State of Delaware (the “DGCL”) regulating corporate takeovers. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging, under certain circumstances, in a business combination with an interested stockholder for a period of three years following the date the person became an interested stockholder unless:

- prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder; or
- 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 commenced, excluding for purposes of determining the voting stock outstanding, but not the outstanding voting stock owned by the interested stockholder, (1) shares owned by persons who are directors and also officers and (2) shares owned by 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
- at or subsequent to the date of the transaction, the business combination is approved by the board of directors of the corporation and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66-2/3% of the outstanding voting stock which is not owned by the interested stockholder.

Generally, a “business combination” includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the “interested stockholder” and an “interested stockholder” is a person who, together with

affiliates and associates, owns or, within three years prior to the determination of interested stockholder status, did own 15% or more of a corporation's outstanding voting stock. We expect the existence of this provision to have an anti-takeover effect with respect to transactions our board of directors does not approve in advance. We also anticipate that Section 203 may discourage business combinations or other attempts that might result in a premium over the market price for the shares of common stock held by our stockholders. The provisions of DGCL, our amended and restated certificate of incorporation, as amended and our amended and restated bylaws could have the effect of discouraging others from attempting hostile takeovers and, as a consequence, they may also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions may also have the effect of preventing changes in our management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock and preferred stock is Broadridge Corporate Issuer Solutions, Inc. The transfer agent's address is 1717 Arch Street, Suite 1300, Philadelphia, Pennsylvania 19103.

DESCRIPTION OF DEPOSITARY SHARES

The following description of the depositary shares does not purport to be complete and is subject to and qualified in its entirety by the relevant deposit agreement and the depositary receipts with respect to the depositary shares relating to any particular series of preferred stock. You should read these documents as they, and not this description, will define your rights as a holder of depositary shares. Forms of these documents will be filed with the SEC in connection with the offering of depositary shares.

General

If we elect to offer fractional interests in shares of preferred stock, we will provide for the issuance by a depositary to the public of receipts for depositary shares. Each depositary share will represent fractional interests of preferred stock. We will deposit the shares of preferred stock underlying the depositary shares under a deposit agreement between us and a bank or trust company selected by us. The bank or trust company must have its principal office in the United States and a combined capital and surplus of at least \$50 million. The depositary receipts will evidence the depositary shares issued under the deposit agreement.

The deposit agreement will contain terms applicable to the holders of depositary shares in addition to the terms stated in the depositary receipts. Each owner of depositary shares will be entitled to all the rights and preferences of the preferred stock underlying the depositary shares in proportion to the applicable fractional interest in the underlying shares of preferred stock. The depositary will issue the depositary receipts to individuals purchasing the fractional interests in shares of the related preferred stock according to the terms of the offering described in a prospectus supplement.

Dividends and Other Distributions

The depositary will distribute all cash dividends or other cash distributions received for the preferred stock to the entitled record holders of depositary shares in proportion to the number of depositary shares that the holder owns on the relevant record date. The depositary will distribute only an amount that can be distributed without attributing to any holder of depositary shares a fraction of one cent. The depositary will add the undistributed balance to and treat it as part of the next sum received by the depositary for distribution to holders of depositary shares.

If there is a non-cash distribution, the depositary will distribute property received by it to the entitled record holders of depositary shares, in proportion, insofar as possible, to the number of depositary shares owned by the

holders, unless the depositary determines, after consultation with us, that it is not feasible to make such distribution. If this occurs, the depositary may, with our approval, sell such property and distribute the net proceeds from the sale to the holders. The deposit agreement also will contain provisions relating to how any subscription or similar rights that we may offer to holders of the preferred stock will be available to the holders of the depositary shares.

Conversion, Exchange, Redemption and Liquidation

If any series of preferred stock underlying the depositary shares may be converted or exchanged, each record holder of depositary receipts will have the right or obligation to convert or exchange the depositary shares represented by the depositary receipts.

The terms on which the depositary shares relating to the preferred stock of any series may be redeemed, and any amounts distributable upon our liquidation, dissolution or winding up, will be described in the relevant prospectus supplement.

Voting

When the depositary receives notice of a meeting at which the holders of the preferred stock are entitled to vote, the depositary will mail the particulars of the meeting to the record holders of the depositary shares. Each record holder of depositary shares on the record date may instruct the depositary on how to vote the shares of preferred stock underlying the holder's depositary shares. The depositary will try, if practical, to vote the number of shares of preferred stock underlying the depositary shares according to the instructions. We will agree to take all reasonable action requested by the depositary to enable it to vote as instructed.

Amendments

We and the depositary may agree to amend the deposit agreement and the depositary receipt evidencing the depositary shares. Any amendment that (a) imposes or increases certain fees, taxes or other charges payable by the holders of the depositary shares as described in the deposit agreement or that (b) otherwise prejudices any substantial existing right of holders of depositary shares, will not take effect until 30 days after the depositary has mailed notice of the amendment to the record holders of depositary shares. Any holder of depositary shares that continues to hold its shares at the end of the 30-day period will be deemed to have agreed to the amendment.

Termination

We may direct the depositary to terminate the deposit agreement by mailing a notice of termination to holders of depositary shares at least 30 days prior to termination. In addition, a deposit agreement will automatically terminate if:

- the depositary has redeemed all related outstanding depositary shares, or
- we have liquidated, terminated or wound up our business and the depositary has distributed the preferred stock of the relevant series to the holders of the related depositary shares.

Payment of Fees and Expenses

We will pay all fees, charges and expenses of the depositary, including the initial deposit of the preferred stock and any redemption of the preferred stock. Holders of depositary shares will pay transfer and other taxes and governmental charges and any other charges as are stated in the deposit agreement for their accounts.

Resignation and Removal of Depositary

At any time, the depositary may resign by delivering notice to us, and we may remove the depositary. Resignations or removals will take effect upon the appointment of a successor depositary and its acceptance of the appointment. The successor depositary must be appointed within 60 days after delivery of the notice of resignation or removal and must be a bank or trust company having its principal office in the United States and having a combined capital and surplus of at least \$50 million.

Reports

The depositary will forward to the holders of depositary shares all reports and communications from us that are delivered to the depositary and that we are required by law, the rules of an applicable securities exchange or our certificate of incorporation to furnish to the holders of the preferred stock. Neither we nor the depositary will be liable if the depositary is prevented or delayed by law or any circumstances beyond its control in performing its obligations under the deposit agreement. The deposit agreement limits our obligations and the depositary's obligations to performance in good faith of the duties stated in the deposit agreement. Neither we nor the depositary will be obligated to prosecute or defend any legal proceeding connected with any depositary shares or preferred stock unless the holders of depositary shares requesting us to do so furnish us with satisfactory indemnity. In performing our obligations, we and the depositary may rely upon the written advice of our counsel or accountants, on any information that competent people provide to us and on documents that we believe are genuine.

DESCRIPTION OF WARRANTS

We may issue warrants for the purchase of debt securities, preferred stock, common stock, depository shares, or any combination thereof. We may issue warrants independently or together with any other securities offered by any prospectus supplement and may be attached to or separate from the other offered securities. Each series of warrants may be issued under a separate warrant agreement to be entered into by us with a warrant agent. The applicable warrant agent will act solely as our agent in connection with the warrants and will not assume any obligation or relationship of agency or trust for or with any holders or beneficial owners of warrants. Further terms of the warrants and the applicable warrant agreements will be set forth in the applicable prospectus supplement.

The applicable prospectus supplement relating to any particular issue of warrants will describe the terms of the warrants, including, as applicable, the following:

- the title of the warrants;
- the aggregate number of the warrants;
- the price or prices at which the warrants will be issued;
- the designation, terms and number of shares of debt securities, preferred stock or common stock purchasable upon exercise of the warrants;
- the designation and terms of the offered securities, if any, with which the warrants are issued and the number of the warrants issued with each offered security;
- the date, if any, on and after which the warrants and the related debt securities, preferred stock or common stock will be separately transferable;
- the price at which each share of debt securities, preferred stock or common stock purchasable upon exercise of the warrants may be purchased;
- the date on which the right to exercise the warrants shall commence and the date on which that right shall expire;
- the minimum or maximum amount of the warrants which may be exercised at any one time;
- information with respect to book-entry procedures, if any;
- a discussion of certain federal income tax considerations; and
- any other terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants.

We and the applicable warrant agent may amend or supplement the warrant agreement for a series of warrants without the consent of the holders of the warrants issued thereunder to effect changes that are not inconsistent with the provisions of the warrants and that do not materially and adversely affect the interests of the holders of the warrants.

DESCRIPTION OF RIGHTS

We may issue rights to purchase common stock or preferred stock. This prospectus and any accompanying prospectus supplement will contain the material terms and conditions for each right. The accompanying prospectus supplement may add, update or change the terms and conditions of the rights as described in this prospectus.

We will describe in the applicable prospectus supplement the terms and conditions of the issue of rights being offered, the rights agreement relating to the rights and the rights certificates representing the rights, including, as applicable:

- the title of the rights;
- the date of determining the stockholders entitled to the rights distribution;
- the title, aggregate number of shares of common stock or preferred stock purchasable upon exercise of the rights;
- the exercise price;
- the aggregate number of rights issued;
- the date, if any, on and after which the rights will be separately transferable;
- the date on which the right to exercise the rights will commence and the date on which the right will expire; and
- any other terms of the rights, including terms, procedures and limitations relating to the distribution, exchange and exercise of the rights.

Each right will entitle the holder of rights to purchase for cash the principal amount of shares of common stock or preferred stock at the exercise price provided in the applicable prospectus supplement. Rights may be exercised at any time up to the close of business on the expiration date for the rights provided in the applicable prospectus supplement. After the close of business on the expiration date, all unexercised rights will be void.

Holders may exercise rights as described in the applicable prospectus supplement. Upon receipt of payment and the rights certificate properly completed and duly executed at the corporate trust office of the rights agent or any other office indicated in the prospectus supplement, we will, as soon as practicable, forward the shares of common stock or preferred stock purchasable upon exercise of the rights. If less than all of the rights issued in any rights offering are exercised, we may offer any unsubscribed securities directly to persons other than stockholders, to or through agents, underwriters or dealers or through a combination of such methods, including pursuant to standby underwriting arrangements, as described in the applicable prospectus supplement.

FORMS OF SECURITIES

Each debt security, depositary share, warrant and right will be represented either by a certificate issued in definitive form to a particular investor or by one or more global securities representing the entire issuance of securities. Unless the applicable prospectus supplement provides otherwise, certificated securities will be issued in definitive form and global securities will be issued in registered form. Definitive securities name you or your nominee as the owner of the security, and in order to transfer or exchange these securities or to receive payments other than interest or other interim payments, you or your nominee must physically deliver the securities to the trustee, registrar, paying agent or other agent, as applicable. Global securities name a depositary or its nominee as the owner of the debt securities, depositary shares, warrants or rights represented by these global securities. The depositary maintains a computerized system that will reflect each investor's beneficial ownership of the securities through an account maintained by the investor with its broker/dealer, bank, trust company or other representative, as we explain more fully below.

Registered Global Securities

We may issue the registered debt securities, depositary shares, warrants and rights in the form of one or more fully registered global securities that will be deposited with a depositary or its nominee identified in the applicable prospectus supplement and registered in the name of that depositary or nominee. In those cases, one or

more registered global securities will be issued in a denomination or aggregate denominations equal to the portion of the aggregate principal or face amount of the securities to be represented by registered global securities. Unless and until it is exchanged in whole for securities in definitive registered form, a registered global security may not be transferred except as a whole by and among the depositary for the registered global security, the nominees of the depositary or any successors of the depositary or those nominees.

If not described below, any specific terms of the depositary arrangement with respect to any securities to be represented by a registered global security will be described in the prospectus supplement relating to those securities. We anticipate that the following provisions will apply to all depositary arrangements.

Ownership of beneficial interests in a registered global security will be limited to persons, called participants, that have accounts with the depositary or persons that may hold interests through participants. Upon the issuance of a registered global security, the depositary will credit, on its book-entry registration and transfer system, the participants' accounts with the respective principal or face amounts of the securities beneficially owned by the participants. Any underwriters, dealers or agents participating in the distribution of the securities will designate the accounts to be credited. Ownership of beneficial interests in a registered global security will be shown on, and the transfer of ownership interests will be effected only through, records maintained by the depositary, with respect to interests of participants, and on the records of participants, with respect to interests of persons holding through participants. The laws of some states may require that some purchasers of securities take physical delivery of these securities in definitive form. These laws may impair your ability to own, transfer or pledge beneficial interests in registered global securities.

So long as the depositary, or its nominee, is the registered owner of a registered global security, that depositary or its nominee, as the case may be, will be considered the sole owner or holder of the securities represented by the registered global security for all purposes under the applicable indenture, deposit agreement, warrant agreement or rights agreement. Except as described below, owners of beneficial interests in a registered global security:

- will not be entitled to have the securities represented by the registered global security registered in their names;
- will not receive or be entitled to receive physical delivery of the securities in definitive form; and
- will not be considered the owners or holders of the securities under the applicable indenture, deposit agreement, warrant agreement or rights agreement.

Accordingly, each person owning a beneficial interest in a registered global security must rely on the procedures of the depositary for that registered global security and, if that person is not a participant, on the procedures of the participant through which the person owns its interest, to exercise any rights of a holder under the applicable indenture, deposit agreement, warrant agreement or rights agreement.

We understand that under existing industry practices, if we request any action of holders or if an owner of a beneficial interest in a registered global security desires to give or take any action that a holder is entitled to give or take under the applicable indenture, deposit agreement, warrant agreement or rights agreement, the depositary for the registered global security would authorize the participants holding the relevant beneficial interests to give or take that action, and the participants would authorize beneficial owners owning through them to give or take that action or would otherwise act upon the instructions of beneficial owners holding through them.

We will make payments of principal, premium, if any, and interest, if any, on debt securities, and any payments to holders with respect to depositary shares, warrants or rights, represented by a registered global security registered in the name of a depositary or its nominee to the depositary or its nominee, as the case may be, as the registered owner of the registered global security. None of us, the trustees, the depositaries for depositary shares, the warrant agents, the rights agents or any other agent of ours, agent of the trustees, agent of

such depositaries, agent of the warrant agents or agent of the rights agents will have any responsibility or liability for any aspect of the records relating to, or payments made on account of, beneficial ownership interests in the registered global security or for maintaining, supervising or reviewing any records relating to those beneficial ownership interests.

We expect that the depositary for any of the securities represented by a registered global security, upon receipt of any payment of principal, premium, interest or other distribution of underlying securities or other property to holders on that registered global security, will immediately credit participants' accounts in amounts proportionate to their respective beneficial interests in that registered global security as shown on the records of the depositary. We also expect that standing customer instructions and customary practices will govern payments by participants to owners of beneficial interests in a registered global security held through the participants, as is now the case with the securities held for the accounts of customers registered in "street name." We also expect that any of these payments will be the responsibility of those participants.

If the depositary for any of the securities represented by a registered global security is at any time unwilling or unable to continue as depositary or ceases to be a clearing agency registered under the Securities Exchange Act of 1934, or Exchange Act, and a successor depositary registered as a clearing agency under the Exchange Act is not appointed by us within 90 days, we will issue securities in definitive form in exchange for the registered global security that had been held by the depositary. Any securities issued in definitive form in exchange for a registered global security will be registered in the name or names that the depositary gives to the relevant trustee, warrant agent, unit agent or other relevant agent of ours or theirs. It is expected that the depositary's instructions will be based upon directions received by the depositary from participants with respect to ownership of beneficial interests in the registered global security that had been held by the depositary.

PLAN OF DISTRIBUTION

We may sell the securities offered by this prospectus to one or more underwriters or dealers for public offering and sale by them or to investors directly or through agents. The accompanying prospectus supplement will set forth the terms of the offering and the method of distribution and will identify any firms acting as underwriters, dealers or agents in connection with the offering, including:

- the name or names of any underwriters, dealers or agents;
- the purchase price of the securities and the proceeds to us from the sale;
- any underwriting discounts and other items constituting compensation to underwriters, dealers or agents;
- any public offering price;
- any discounts or concessions allowed or reallocated or paid to dealers; and
- any securities exchange or market on which the securities offered in the prospectus supplement may be listed.

Only those underwriters identified in such prospectus supplement are deemed to be underwriters in connection with the securities offered in the prospectus supplement.

The distribution of the securities may be effected from time to time in one or more transactions at a fixed price or prices, which may be changed, or at prices determined as the applicable prospectus supplement specifies. The securities may be sold through an at-the-market offering, a rights offering, forward contracts or similar arrangements. In addition, we may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement so indicates, in connection with those derivatives, the third parties may sell securities covered by this

prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter and, if not identified in this prospectus, will be named in the applicable prospectus supplement (or a post-effective amendment). In addition, we may otherwise loan or pledge securities to a financial institution or other third party that in turn may sell the securities short using this prospectus and an applicable prospectus supplement. Such financial institution or other third party may transfer its economic short position to investors in our securities or in connection with a concurrent offering of other securities.

In connection with the sale of the securities, underwriters, dealers or agents may be deemed to have received compensation from us in the form of underwriting discounts or commissions and also may receive commissions from securities purchasers for whom they may act as agent. Underwriters may sell the securities to or through dealers, and the dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters or commissions from the purchasers for whom they may act as agent.

We will provide in the applicable prospectus supplement information regarding any underwriting discounts or other compensation that we pay to underwriters or agents in connection with the securities offering, and any discounts, concessions or commissions that underwriters allow to dealers. Underwriters, dealers and agents participating in the securities distribution may be deemed to be underwriters, and any discounts, commissions or concessions they receive and any profit they realize on the resale of the securities may be deemed to be underwriting discounts and commissions under the Securities Act of 1933. Underwriters and their controlling persons, dealers and agents may be entitled, under agreements entered into with us, to indemnification against and contribution toward specific civil liabilities, including liabilities under the Securities Act. Some of the underwriters, dealers or agents who participate in the securities distribution may engage in other transactions with, and perform other services for, us or our subsidiaries in the ordinary course of business.

Our common stock is currently listed on the Nasdaq Capital Market, but any other securities may or may not be listed on a national securities exchange. To facilitate the offering of securities, certain persons participating in the offering may engage in transactions that stabilize, maintain or otherwise affect the price of the securities. This may include over-allotments or short sales of the securities, which involve the sale by persons participating in the offering of more securities than were sold to them. In these circumstances, these persons would cover such over-allotments or short positions by making purchases in the open market or by exercising their over-allotment option, if any. In addition, these persons may stabilize or maintain the price of the securities by bidding for or purchasing securities in the open market or by imposing penalty bids, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if securities sold by them are repurchased in connection with stabilization transactions. The effect of these transactions may be to stabilize or maintain the market price of the securities at a level above that which might otherwise prevail in the open market. These transactions may be discontinued at any time.

LEGAL MATTERS

The validity of any securities offered by this prospectus will be passed upon for us by Pillsbury Winthrop Shaw Pittman LLP, Palo Alto, California.

EXPERTS

The consolidated financial statements as of December 31, 2019 and 2018 and for the years then incorporated by reference in this prospectus and in the registration statement have been so incorporated in reliance on the report of BDO USA, LLP, an independent registered public accounting firm (the report on the consolidated financial statements contains an explanatory paragraph regarding the Company's ability to continue as a going concern), incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We have filed a registration statement on Form S-3 with the SEC under the Securities Act of 1933. This prospectus is part of the registration statement but the registration statement includes and incorporates by reference additional information and exhibits. We file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC maintains a web site that contains reports, proxy and information statements and other information regarding companies, such as ours, that file documents electronically with the SEC. The address of that site on the worldwide web is <http://www.sec.gov>. The information on the SEC's web site is not part of this prospectus, and any references to this web site or any other web site are inactive textual references only.

INCORPORATION BY REFERENCE

The SEC permits us to "incorporate by reference" the information contained in documents we file with the SEC, which means that we can disclose important information to you by referring you to those documents rather than by including them in this prospectus. Information that is incorporated by reference is considered to be part of this prospectus and you should read it with the same care that you read this prospectus. Later information that we file with the SEC will automatically update and supersede the information that is either contained, or incorporated by reference, in this prospectus, and will be considered to be a part of this prospectus from the date those documents are filed. We have filed with the SEC, and incorporate by reference in this prospectus:

- our Annual Report on [Form 10-K](#) and [Form 10-K/A](#) for the year ended December 31, 2019 (filed with the SEC on March 30, 2020 and April 29, 2020, respectively);
- our Quarterly Reports on Form 10-Q for the quarters ended [March 31, 2020](#) and [June 30, 2020](#) (filed with the SEC on May 14, 2020 and August 10, 2020, respectively);
- our Current Reports on Form 8-K filed with the SEC on [January 3, 2020](#), [February 6, 2020](#), [March 12, 2020](#), [March 30, 2020](#), [April 23, 2020](#), [June 11, 2020](#), [June 17, 2020](#), [August 4, 2020](#), [September 15, 2020](#), [October 5, 2020](#), and [October 6, 2020](#) (to the extent filed and not furnished); and
- the description of our common stock contained in our Registration Statement on [Form 10/A](#) filed on July 16, 2001, and any amendment or report filed with the Commission for the purpose of updating the description.

We also incorporate by reference all additional documents that we file with the SEC under the terms of Section 13(a), 13(c), 14 or 15(d) of the Exchange Act that are made after the initial filing date of the registration statement of which this prospectus is a part and the effectiveness of the registration statement, as well as between the date of this prospectus and the termination of any offering of securities offered by this prospectus (excluding any portions thereof furnished by the Registrant, including but not limited to information furnished under Item 2.02 and Item 7.01 and any exhibits relating to Item 2.02 or Item 7.01 furnished under Item 9.01 of Form 8-K and any certification required by 18 U.S.C. § 1350).

Any statement contained in this Registration Statement or in a document incorporated by reference in this Registration Statement shall be deemed to be modified or superseded for purposes of this Registration Statement to the extent that a statement contained in this Registration Statement or in any subsequently filed document that is deemed to be incorporated by reference in this Registration Statement modifies or supersedes such statement.

You may request a copy of any or all of the documents incorporated by reference but not delivered with this prospectus, at no cost, by writing or telephoning us at the following address and number: Plus Therapeutics, Inc., 4200 Marathon Blvd., Suite 200, Austin, Texas 78756, telephone (737) 255-7194. We will not, however, send exhibits to those documents, unless the exhibits are specifically incorporated by reference in those documents.

We make available free of charge on our website our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports, as soon as reasonably practicable after we electronically file or furnish such materials to the Securities and Exchange Commission, or SEC. You may obtain a free copy of these reports in the Investor Relations section of our website, www.plustherapeutics.com.

\$5,040,000



Common Stock

PROSPECTUS SUPPLEMENT

Canaccord Genuity