

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

**Form S-1
REGISTRATION STATEMENT
Under
The Securities Act of 1933**

PLUS THERAPEUTICS, INC.

(Exact name of Registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

2834
(Primary Standard Industrial
Classification Code Number)

33-0827593
(I.R.S. Employer
Identification Number)

4200 Marathon Blvd., Suite 200
Austin, TX 78756
(737)-255-7194

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

Andrew Sims
Chief Executive Officer
Plus Therapeutics, Inc.
4200 Marathon Blvd., Suite 200
Austin, TX 78756
(737)-255-7194

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

Copies to:

Andrew L. Strong
Davina K. Kaile
Pillsbury Winthrop Shaw Pittman LLP
2 Houston Center – 909 Fannin, Suite 2000
Houston, TX 77010
(713) 276-7677

Approximate date of commencement of proposed sale to the public: From time to time after this registration statement becomes effective, as determined by the selling stockholder.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act, check the following box:

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

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

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

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

Large accelerated filer

Accelerated filer

Non-accelerated filer

Smaller reporting company

Emerging growth company

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

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to be Registered ⁽¹⁾	Proposed Maximum Offering Price Per Share ⁽²⁾	Proposed Maximum Aggregate Offering Price ⁽²⁾	Amount of Registration Fee
Common Stock, par value \$0.001 per share	4,500,000	\$3.16	\$14,220,000	\$1,552

(1) Represents 4,500,000 shares of common stock that are issuable pursuant to a purchase agreement with the selling stockholder named herein. Pursuant to Rule 416(a) under the Securities Act of 1933, the registrant is also registering hereunder an indeterminate number of shares that may be issued and resold resulting from stock splits, stock dividends or similar transactions.

(2) Estimated pursuant to Rule 457(c) solely for the purpose of calculating the registration fee, based upon the average of the high and low prices for the registrant's common stock as reported on the Nasdaq Capital Market on February 24, 2021.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with the provisions of Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

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

PRELIMINARY PROSPECTUS

(Subject to Completion, Dated February 26, 2021)

4,500,000 Shares of Common Stock



This prospectus relates to the offer and sale of up to 4,500,000 shares of our common stock, par value \$0.001 per share, by Lincoln Park Capital Fund, LLC, which we refer to in this prospectus as Lincoln Park or the selling stockholder.

The shares of common stock to which this prospectus relates may be issued by us to Lincoln Park pursuant to a purchase agreement, dated as of September 30, 2020, we entered into with Lincoln Park, which we refer to in this prospectus as the Purchase Agreement. We are not selling any securities under this prospectus and will not receive any of the proceeds from the sale of our common stock by the selling stockholder. However, we may receive up to \$25.0 million aggregate gross proceeds under the Purchase Agreement from sales of common stock to Lincoln Park pursuant to the Purchase Agreement, including sales of our common stock to Lincoln Park under the Purchase Agreement that were completed prior to the date of this prospectus and sales of our common stock to Lincoln Park we may make from time to time from and after the date of this prospectus. On October 2, 2020, we issued 180,701 shares to Lincoln Park as consideration for its irrevocable commitment to purchase our common stock under the Purchase Agreement, which we refer to in this prospectus as the Commitment Shares. As of February 11, 2021, we have sold an aggregate of 1,338,299 shares of our common stock to Lincoln Park under the Purchase Agreement, which shares (together with the 180,701 Commitment Shares) were registered for resale by Lincoln Park under a separate registration statement that we previously filed with the Securities and Exchange Commission, or the SEC, which was declared effective by the SEC on November 5, 2020. See “The Lincoln Park Transaction” for a description of the Purchase Agreement and “Selling Stockholder” for additional information regarding Lincoln Park.

The selling stockholder may sell or otherwise dispose of the common stock described in this prospectus in a number of different ways and at varying prices. See “Plan of Distribution” for more information about how the selling stockholder may sell or otherwise dispose of the common stock being registered pursuant to this prospectus. The selling stockholder is an “underwriter” within the meaning of Section 2(a)(11) of the Securities Act of 1933, as amended, or the Securities Act.

We will pay the expenses incurred in registering under the Securities Act the offer and sale of the common stock to which this prospectus relates by the selling stockholder, including legal and accounting fees. See “Plan of Distribution”.

Our common stock is currently listed on the Nasdaq Capital Market, or Nasdaq, under the symbol “PSTV.” On February 24, 2021, the closing price of our common stock, as reported on Nasdaq, was \$3.08 per share.

Investing in our securities involves a high degree of risk. These risks are described in the “[Risk Factors](#)” section on page 9 of this prospectus. You should also consider the risk factors described or referred to in any documents incorporated by reference in this prospectus, and in any applicable prospectus supplement, before investing in these securities.

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

The date of this prospectus is _____, 2021

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ABOUT THIS PROSPECTUS

This prospectus forms part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, and that 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, together with the additional information described under the headings “Where You Can Find More Information” and “Incorporation by Reference” before making your investment decision.

You should rely only on the information provided in this prospectus or in a prospectus supplement or any free writing prospectuses or amendments thereto. Neither we, nor the selling stockholder, have authorized anyone else to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. You should assume that the information in this prospectus is accurate only as of the date hereof. Our business, financial condition, results of operations and prospects may have changed since that date.

Neither we, nor the selling stockholder, are offering to sell or seeking offers to purchase these securities in any jurisdiction where the offer or sale is not permitted. We have not done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the securities as to distribution of the prospectus outside of the United States.

Unless the context otherwise requires, references in this prospectus to “Plus,” “the Company,” “we,” “us” and “our” refer to Plus Therapeutics, Inc. Our logo and all product names are our common law trademarks. Solely for convenience, trademarks and tradenames referred to in this prospectus may appear without the ® or ™ symbols, but such references are not intended to indicate in any way that we will not assert, to the fullest extent under applicable law, our rights, or that the applicable owner will not assert its rights, to these trademarks and tradenames.

PROSPECTUS SUMMARY

This summary contains basic 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 you decide to invest in our common stock, you should read this entire prospectus carefully, including the section entitled "Risk Factors," and any documents incorporated by reference.

Our Business

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.

Summary Risk Factors

Below is a summary of the principal factors that may affect our business, financial condition, and results of operations. This summary does not address all of the risks that we face. Additional discussion of the risks summarized in this risk factor summary, and other risks that we face, can be found below under the heading “Risk Factors” and should be carefully considered, together with other information in our Annual Report Form 10-K and our other filings with the SEC.

- We have incurred losses since inception and expect to incur significant net losses in the foreseeable future and therefore may never become profitable.
- We will need substantial additional funding to develop our product candidates and conduct our future operations and to repay our outstanding debt obligations. If we are unable to obtain the funds necessary to do so, we may be required to delay, scale back or eliminate our product development activities or may be unable to continue our business operations.
- Our indebtedness to Oxford could adversely affect our operations and liquidity. The disruption and volatility in the global capital markets may negatively impact our ability to obtain additional debt financings and modify our existing debt facilities and may increase the risk of non-compliance with covenants under our existing loan agreement.
- 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”.
- Our operating results have been and will likely continue to be volatile.
- Our future success is in large part dependent upon our ability to successfully integrate and develop our nanomedicine platform and commercialize RNL and any failure to do so could significantly harm our business and prospects.
- If we are unable to successfully partner with other companies to commercialize our product candidates, our business could materially suffer.
- Our current business strategy is high-risk and may not be successful.
- We face intense competition, and if our competitors market or develop products that are marketed more effectively, approved more quickly than our product candidates, or demonstrated to be safer or more effective than our product candidates, our commercial opportunities could be reduced or eliminated.
- Our current and future clinical trials may fail to demonstrate acceptable levels of safety and efficacy for our product candidate, which could prevent or significantly delay their regulatory approval and commercialization, which would have a material and adverse impact on our business.
- We rely on third parties to conduct our clinical trials, manufacture our product candidates, and perform other services. If these parties are not able to successfully perform due to the impact of the COVID-19 pandemic or otherwise, we may not be able to successfully complete clinical development, obtain regulatory approval or commercialize our product candidates and our business could be substantially harmed.
- We may have difficulty enrolling, or fail to enroll patients, in our clinical trials, which could delay or prevent clinical trials of our drug candidates.

- Our success depends in substantial part on our ability to obtain regulatory approvals for our RNL product candidate. However, we cannot be certain that we will receive regulatory approval for this product candidate or our other product candidates.
- If we or collaborators fail to comply with regulatory requirements applicable to the development, manufacturing, and marketing of our product candidates, regulatory agencies may take action against us or them, which could significantly harm our business.
- We and our product candidates are subject to extensive regulation, and the requirements to obtain regulatory approvals in the United States and other jurisdictions can be costly, time-consuming and unpredictable. If we or our partners are unable to obtain timely regulatory approval for our product candidates, our business may be substantially harmed.
- If we are unable to identify, hire and/or retain key personnel, or if any of our personnel were to test positive for COVID-19, we may not be able to sustain or grow our business.
- We face potential product liability exposure, and if successful claims are brought against us, we may incur substantial liability if our insurance coverage for those claims is inadequate.
- We and our collaborators must comply with environmental laws and regulations, including those pertaining to use of hazardous and biological materials in our business, and failure to comply with these laws and regulations could expose us to significant liabilities.
- Our success depends in part on our ability to protect our intellectual property.
- We may incur substantial costs as a result of litigation or other proceedings relating to patent and other intellectual property rights, and we may be unable to protect our rights to our product candidates and technology.
- If we are sued for infringing intellectual property rights of third parties, it will be costly and time consuming, and an unfavorable outcome in that litigation would have a material adverse effect on our business.
- We may issue debt and equity securities or securities convertible into equity securities, any of which may be senior to our common stock as to distributions and in liquidation, which could negatively affect the value of our common stock.
- We could be delisted from Nasdaq, which would seriously harm the liquidity of our stock and our ability to raise capital.
- If securities and/or industry analysts fail to continue publishing research about our business, if they change their recommendations adversely, or if our results of operations do not meet their expectations, our stock price and trading volume could decline.
- The COVID-19 pandemic could adversely affect our business, results of operations, and financial condition.
- We may face business disruption and related risks resulting from the COVID-19 pandemic and the invocation of the Defense Production Act, either of which could have a material adverse effect on our business.
- We may not have access to the full amount available under the Purchase Agreement with Lincoln Park. We may require additional financing to sustain our operations, without which we may not be able to continue operations, and the terms of subsequent financings may adversely impact our stockholders.

The Purchase Agreement with Lincoln Park

On September 30, 2020, we entered into the Purchase Agreement with Lincoln Park, pursuant to which Lincoln Park has agreed to purchase from us up to an aggregate of \$25.0 million of our common stock (subject to

certain limitations) from time to time over the term of the Purchase Agreement. Also on September 30, 2020, we entered into a registration rights agreement with Lincoln Park, which we refer to in this prospectus as the Registration Rights Agreement, pursuant to which we filed with the SEC the registration statement that includes this prospectus to register for resale under the Securities Act of 1933, as amended, or the Securities Act, the shares of our common stock that may be issued to Lincoln Park under the Purchase Agreement.

We previously filed a registration statement on Form S-1 (File No. 333-249728) that was declared effective by the SEC on November 5, 2020, which we refer to as the Prior Registration Statement, covering the resale by the selling stockholder of up to 1,519,000 shares of our common stock, comprised of: (i) 180,701 Commitment Shares that we issued to Lincoln Park on October 2, 2020 as a fee for making its irrevocable commitment to purchase our common stock under the Purchase Agreement, and (ii) up to an additional 1,338,299 shares of our common stock that we had reserved for issuance and sale to Lincoln Park under the Purchase Agreement from time to time from and after the date on which all the conditions set forth in the Purchase Agreement, including that the Prior Registration Statement be declared effective by the SEC, were satisfied, all of which conditions were satisfied on November 5, 2020 (the “Commencement Date”). From the Commencement Date through February 11, 2021, we sold an aggregate of 1,338,299 shares of our common stock to Lincoln Park under the Purchase Agreement, exhausting all of the shares of common stock that were previously registered for resale by Lincoln Park on the Prior Registration Statement. This prospectus covers the resale of up to an additional 4,500,000 shares of our common stock that we have reserved for issuance and sale to Lincoln Park under the Purchase Agreement from time to time from and after the date of this prospectus, if and when we determine to sell additional shares of our common stock to Lincoln Park under the Purchase Agreement.

Other than the 180,701 Commitment Shares that we issued to Lincoln Park as a fee for making its irrevocable commitment to purchase our common stock under the Purchase Agreement, we did not have the right to commence sales of our common stock to Lincoln Park under the Purchase Agreement until the Commencement Date. From and after the Commencement Date, we may, from time to time and at our sole discretion for a period of 36 months after the Commencement Date, on any business day that we select on which the closing sale price of our common stock equals or exceeds \$0.25 per share, direct Lincoln Park to purchase up to 50,000 shares of our common stock, which amount may be increased depending on the market price of our common stock at the time of sale, subject to a maximum commitment of \$500,000 per purchase, which we refer to in this prospectus as “Regular Purchases.” In addition, at our discretion, Lincoln Park has committed to purchase other “accelerated amounts” and/or “additional accelerated amounts” under certain circumstances. We will control the timing and amount of any sales of our common stock to Lincoln Park. The purchase price of the shares of our common stock that have been sold and may be sold to Lincoln Park in Regular Purchases under the Purchase Agreement was and will be based on the market price of our common stock preceding the time of sale as computed under the Purchase Agreement. The purchase price per share will be equitably adjusted as provided in the Purchase Agreement for any reorganization, recapitalization, non-cash dividend, stock split, or other similar transaction as set forth in the Purchase Agreement. We may at any time in our sole discretion terminate the Purchase Agreement without fee, penalty or cost upon one business day notice. There are no restrictions on future financings, rights of first refusal, participation rights, penalties or liquidated damages in the Purchase Agreement or Registration Rights Agreement, other than a prohibition on our entering into certain types of transactions that are defined in the Purchase Agreement as “Variable Rate Transactions.” Lincoln Park may not assign or transfer its rights and obligations under the Purchase Agreement.

As of February 24, 2021, there were 9,166,902 shares of our common stock outstanding, of which 9,129,988 shares of our common stock were held by non-affiliates. The 9,166,902 shares of our common stock outstanding as of February 24, 2021 includes 1,338,299 shares previously issued and sold to Lincoln Park under the Purchase Agreement. If all of the 4,500,000 shares offered by Lincoln Park under this prospectus were issued and outstanding, such shares would represent approximately 32.9% of the total number of shares of our common stock outstanding and approximately 33.0% of the total number of outstanding shares held by non-affiliates, in

each case as of February 24, 2021. The Purchase Agreement provides that we may sell up to an aggregate of \$25.0 million of our common stock to Lincoln Park. As of February 11, 2021, we have sold an aggregate of 1,338,299 shares of our common stock to Lincoln Park under the Purchase Agreement for an aggregate of approximately \$3.6 million, all of which shares (together with the 180,701 Commitment Shares) were registered for resale by Lincoln Park under the Prior Registration Statement. Since we have previously issued and sold to Lincoln Park all of the shares of common stock that were registered for resale by Lincoln Park under the Prior Registration Statement, we have filed the registration statement that includes this prospectus so that we may issue and sell to Lincoln Park up to an additional 4,500,000 shares of our common stock from time to time from and after the date of this prospectus. Depending on the market prices of our common stock at the time we elect to issue and sell such additional shares to Lincoln Park under the Purchase Agreement, we may need to sell more shares to Lincoln Park than are offered under this prospectus to receive aggregate gross proceeds equal to the \$21.4 million balance of the \$25.0 million total commitment of Lincoln Park under the Purchase Agreement, in which case we must first register for resale under the Securities Act additional shares of our common stock, which could cause additional substantial dilution to our stockholders. The number of shares ultimately offered for resale by Lincoln Park is dependent upon the number of shares we sell to Lincoln Park under the Purchase Agreement.

Under applicable Nasdaq rules, in no event may we issue or sell to Lincoln Park under the Purchase Agreement shares of our common stock in excess of 917,823 shares (including the Commitment Shares), which represents 19.99% of the shares of our common stock outstanding (based on 4,591,415 shares outstanding) immediately prior to the execution of the Purchase Agreement, which limitation we refer to as the Exchange Cap, unless (i) we obtain stockholder approval to issue shares of our common stock in excess of the Exchange Cap or (ii) the average price of all applicable sales of our common stock to Lincoln Park under the Purchase Agreement equals or exceeds \$3.1872 per share (which represents the lower of (A) the official closing price of our common stock on Nasdaq on the trading day immediately preceding the date of the Purchase Agreement and (B) the average official closing price of our common stock on Nasdaq for the five consecutive trading days ending on the trading day immediately preceding the date of the Purchase Agreement, plus an incremental amount of \$0.6272 attributable to the value of the Commitment Shares), so that such issuances and sales would be exempt from the Exchange Cap limitation under applicable Nasdaq rules. In any event, the Purchase Agreement specifically provides that we may not issue or sell any shares of our common stock under the Purchase Agreement if such issuance or sale would breach any applicable rules or regulations of The Nasdaq Stock Market.

Prior to entering into the Purchase Agreement with Lincoln Park, on June 16, 2020, we received stockholder approval on June 16, 2020 pursuant to Nasdaq Listing Rules 5635(a), 5635(b) and 5635(d) to permit issuances of our common stock (including the issuance of more than 19.99% of our common stock) to Lincoln Park pursuant to the Purchase Agreement. Based on the closing price of our common stock of \$1.05 per share on March 16, 2020 (the lowest closing sale price since January 1, 2020 as reported on Nasdaq.com), the maximum number of shares we can issue and sell under the Purchase Agreement is approximately 23.8 million shares. Accordingly, we requested and received stockholder approval for the issuance of up to 23.8 million shares of our common stock in the aggregate under the Purchase Agreement. We would seek additional stockholder approval before issuing more than an aggregate of 23.8 million shares under the Purchase Agreement.

The Purchase Agreement also prohibits us from directing Lincoln Park to purchase any shares of common stock if those shares, when aggregated with all other shares of our common stock then beneficially owned by Lincoln Park and its affiliates, would result in Lincoln Park and its affiliates having beneficial ownership, at any single point in time, of more than 4.99% of the then total outstanding shares of our common stock, as calculated pursuant to Section 13(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and Rule 13d-3 thereunder, which limitation we refer to as the Beneficial Ownership Cap.

There are substantial risks to our stockholders as a result of the sale and issuance of common stock to Lincoln Park under the Purchase Agreement. These risks include substantial dilution, significant declines in our stock price and our inability to draw sufficient funds when needed. See “Risk Factors.” The sale of our common stock to Lincoln Park under the Purchase Agreement will not affect the rights or privileges of our other stockholders, except that the economic and voting interests of our existing stockholders will be diluted as a result of any such sale. Although the number of shares of common stock that our other stockholders own will not decrease, the shares owned by our other stockholders will represent a smaller percentage of our total outstanding shares after any such sale to Lincoln Park under the Purchase Agreement.

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 and the references in this prospectus and the documents we have incorporated by reference to our website do not constitute incorporation by reference into this prospectus of the information contained therein.

THE OFFERING

Shares of our common stock offered by the selling stockholder	Up to 4,500,000 shares of our common stock that we may issue and sell to Lincoln Park from time to time under the Purchase Agreement.
Shares of our common stock outstanding prior to this offering (as of February 24, 2021)	9,166,902 shares of our common stock.
Shares of our common stock to be outstanding after this offering	13,666,902 shares of our common stock, assuming the sale of a total of 4,500,000 shares of common stock to Lincoln Park. The actual number of shares outstanding after this offering will vary depending upon the actual number of shares we sell to Lincoln Park under the Purchase Agreement after the date of this prospectus.
Use of proceeds	We will receive no proceeds from the sale of shares of our common stock by Lincoln Park in this offering. We may receive up to \$25.0 million aggregate gross proceeds under the Purchase Agreement from any sales of shares of our common stock we make to Lincoln Park pursuant to the Purchase Agreement, assuming that we sell the full amount of our common stock that we have the right, but not the obligation to sell to Lincoln Park under the Purchase Agreement. Any proceeds that we receive from sales of shares of our common stock to Lincoln Park under the Purchase Agreement will be used for working capital and general corporate purposes. See “Use of Proceeds.”
Nasdaq symbol for our common stock	“PSTV”
Risk factors	This investment involves a high degree of risk. See “Risk Factors” beginning on page 9 of this prospectus for a discussion of factors you should carefully consider before deciding to invest in our securities.

Unless otherwise noted, the number of shares of common stock to be outstanding immediately after this offering 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;
- 210,389 shares of common stock reserved for future issuance under our 2015 New Employee Incentive Plan; and
- 159,939 shares of common stock reserved for future issuance under our 2020 Stock 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; and
- 3,113,625 shares of common stock issuable upon the exercise of warrants to purchase common stock, with a weighted-average exercise price of \$2.62 per share.

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During 2021 and through the date of this prospectus, we issued and sold 985,186 shares of our common stock under the Purchase Agreement for net proceeds of \$2.9 million, and issued 536,070 shares under an Equity Distribution Agreement (the “Distribution Agreement”) with Canaccord Genuity LLC (“Canaccord”) for net proceeds of \$1.5 million. In February 2021, certain warrant holders exercised warrants to purchase 896,500 shares of our common stock for total exercise proceeds of \$2.0 million. 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, it could result in further dilution to our stockholders.

RISK FACTORS

Investing in our securities involves a high degree of risk. Before making an investment decision with respect to our securities, we urge you to carefully consider the risks described below and in the “Risk Factors” sections of our most recent Annual Report on Form 10-K and Quarterly Reports on Form 10-Q, as well as our Current Reports on Form 8-K, filed with the SEC and incorporated by reference in this prospectus, and the other information contained in this prospectus. The risks and uncertainties incorporated by reference into this prospectus or described below are not the only ones we face. Additional risks and uncertainties not presently known or which we consider immaterial as of the date hereof may also materially harm our business and could result in a complete loss of your investment. If any of the matters discussed in the following risk factors were to occur, our business, financial condition, results of operations, cash flows, or prospects could be materially and adversely affected, the market price of our common stock could decline, and you could lose all or part of your investment in our securities.

Risks Related to the 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 revenue 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.

The sale or issuance of our common stock to Lincoln Park may cause dilution to our other stockholders 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.

Lincoln Park has committed to purchase up to \$25.0 million of our common stock under the Purchase Agreement. As of February 11, 2021, we have sold an aggregate of 1,338,299 shares of our common stock to Lincoln Park under the Purchase Agreement for an aggregate of approximately \$3.6 million, leaving approximately \$21.4 million balance of the \$25.0 million total commitment of Lincoln Park under the Purchase Agreement. The purchase price for the shares that we may sell to Lincoln Park under the Purchase Agreement remains subject to the pricing formula in the Purchase Agreement and will fluctuate based on the price of our common stock. Depending on market liquidity at the time, any future 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 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

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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 additional shares to Lincoln Park, after Lincoln Park has acquired the shares, Lincoln Park may resell all, some or none of those shares at any time or from time to time in its discretion. Therefore, additional 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.

We may not have access to the full amount available under the Purchase Agreement with Lincoln Park. We may require additional financing to sustain our operations, without which we may not be able to continue operations, and the terms of subsequent financings may adversely impact our stockholders.

We may direct Lincoln Park to purchase up to \$25.0 million worth of shares of our common stock from time to time under the Purchase Agreement over a 36-month period generally in amounts up to 50,000 shares of our common stock, which may be increased to up to 100,000 shares of our common stock depending on the market price of our common stock at the time of sale, provided that Lincoln Park's committed obligation under such single Regular Purchase shall not exceed \$500,000. Through December 31, 2020, we have sold a total of 353,113 shares, excluding 180,701 shares issued for commitment fee, under the Purchase Agreement for net proceeds of \$0.7 million. During 2021 and through February 11, 2021, we issued and sold 985,186 shares of our common stock under the Purchase Agreement for net proceeds of \$2.9 million, leaving a balance of approximately \$21.4 million of the \$25.0 million total commitment from Lincoln Park.

Depending on the prevailing market price of our common stock, we may not be able to sell shares to Lincoln Park for the maximum \$25.0 million over the term of the Purchase Agreement. We obtained stockholder approval to issue up to 23.8 million shares of common stock at our 2020 annual stockholders' meeting, so are not constrained by the Nasdaq limit of 19.99% of our outstanding shares that might otherwise apply. However, we will need to seek additional stockholder approval before issuing more than 23.8 million shares. We are not required or permitted to issue any shares of common stock under the Purchase Agreement if such issuance would breach our obligations under the rules or regulations of The Nasdaq Stock Market. In addition, Lincoln Park will not be required to purchase any shares of our common stock if such sale would result in Lincoln Park's beneficial ownership exceeding 4.99% of the then outstanding shares of our common stock. Our inability to access a portion or the full amount available under the Purchase Agreement, in the absence of any other financing sources, could have a material adverse effect on our business.

The extent we rely on Lincoln Park as a source of funding will depend on a number of factors, including the prevailing market price of our common stock and the extent to which we are able to secure working capital from other sources. If obtaining sufficient funding from Lincoln Park were to prove unavailable or prohibitively dilutive, we will need to secure another source of funding in order to satisfy our working capital needs. Even if we sell all \$25.0 million of shares of our common stock under the Purchase Agreement to Lincoln Park, we may still need additional capital to finance our future production plans and working capital needs, and we may have to raise funds through the issuance of equity or debt securities. Assuming a purchase price of \$3.08 (which represents the closing price of our common stock on February 24, 2021), the purchase by Lincoln Park of the entire 4,500,000 additional shares being registered hereunder would result in gross proceeds to us of only approximately \$13.9 million, which together with the \$3.6 million we sold to Lincoln Park under the Purchase Agreement between the Commencement Date and February 11, 2021, would result in total gross proceeds to us of \$17.5 million of the \$25.0 million total commitment under the Purchase Agreement.

Depending on the type and the terms of any financing we pursue, stockholders' rights and the value of their investment in our common stock could be reduced. A financing could involve one or more types of securities including common stock, convertible debt or warrants to acquire common stock. These securities could be issued at or below the then prevailing market price for our common stock. In addition, if we issue secured debt securities, the holders of the debt would have a claim to our assets that would be prior to the rights of

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stockholders until the debt is paid. Interest on these debt securities would increase costs and negatively impact operating results. If the issuance of new securities results in diminished rights to holders of our common stock, the market price of our common stock could be negatively impacted.

Should the financing we require to sustain our working capital needs be unavailable or prohibitively expensive when we require it, the consequences could be a material adverse effect on our business, operating results, financial condition and prospects.

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

Our management will have broad discretion as to the use of the net proceeds from our sale of shares of common stock to Lincoln Park, 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.

Risks Related to our Business and Industry

We will need substantial additional funding to develop our products and conduct our future operations and to repay our outstanding debt obligations. If we are unable to obtain the funds necessary to do so, we may be required to delay, scale back or eliminate our product development activities or may be unable to continue our business operations

We have had, and we will continue to have, an ongoing need to raise additional cash from outside sources to continue funding our operations, including our continuing substantial research and development expenses. We do not currently believe that our cash balance will be sufficient to fund the development and marketing efforts required to reach profitability without raising additional capital from accessible sources of financing in the near future. Our future capital requirements will depend on many factors, including:

- our ability to raise capital to fund our operations on terms acceptable to us, or at all;
- our perceived capital needs with respect to our development programs, and any delays in, adverse events and excessive costs of such programs beyond what we currently anticipate;
- our ability to establish and maintain collaborative and other arrangements with third parties to assist in bringing our products to market and the cost of such arrangements at the time;
- costs associated with operating at our San Antonio, Texas facility;
- the cost of manufacturing our product candidates, including compliance with good manufacturing practices applicable to our product candidates;
- expenses related to the establishment of sales and marketing capabilities for product candidates awaiting approval or products that have been approved;
- competing technological and market developments; and
- our ability to introduce and sell new products.

We will continue to require substantial additional capital to continue our clinical development and potential commercialization activities. Accordingly, we will need to raise substantial additional capital to continue to fund

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our operations. Our financing plans include seeking to raise additional cash through the use of debt and/or equity offering programs, strategic corporate partnerships, state and federal development programs, licensing, and sales of assets and equity. The amount and timing of our future funding requirements will depend on many factors, including the pace and results of its clinical development efforts.

We have secured capital historically from grant revenue, collaboration proceeds, and debt and equity offerings. To obtain additional capital, we may pursue debt and/or equity offering programs, strategic corporate partnerships, state and federal development programs, licensing arrangements, and sales of assets or debt or equity securities. We cannot be certain that additional capital will be available on terms acceptable to us, or at all. 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 curtailment or cessation of operations.

In addition, on October 23, 2020, we entered into the “Distribution Agreement with Canaccord, pursuant to which we may issue and sell, from time to time, shares of our common stock having an aggregate offering price of up to \$10,000,000 (the “ATM Shares”), depending on market demand, with Canaccord acting as an agent for sales. Sales of the ATM Shares may be made by any method permitted by law deemed to be an “at the market offering” as defined in Rule 415(a)(4) of the Securities Act of 1933, as amended (the “Securities Act”), including, without limitation, sales made directly on or through the Nasdaq Capital Market. Canaccord will use its commercially reasonable efforts to sell the ATM Shares we request to be sold on our behalf, consistent with Canaccord’s normal trading and sales practices, under the terms and subject to the conditions set forth in the Distribution Agreement. We have no obligation to sell any of the ATM Shares. We may instruct Canaccord not to sell the ATM Shares if the sales cannot be effected at or above the price we designate from time to time and we may at any time suspend sales pursuant to the Distribution Agreement.

Failure to raise capital as and when needed, on favorable terms or at all, would have a significant negative impact on our financial condition and our ability to develop our product candidates.

Our indebtedness to Oxford could adversely affect our operations and liquidity. The disruption and volatility in the global capital markets may negatively impact our ability to obtain additional debt financings and modify our existing debt facilities and may increase the risk of non-compliance with covenants under our existing loan agreement.

Under the Loan and Security Agreement, dated May 29, 2015 (the “Loan and Security Agreement”), as amended, with Oxford Finance, LLC (“Oxford”), Oxford made a term loan to us in an aggregate principal amount of \$17.7 million (the “Term Loan”) subject to the terms and conditions set forth therein. As of December 31, 2020, the outstanding principal balance of the Term Loan was \$4.3 million subsequent to a repayment of \$5.0 million on April 1, 2020 pursuant to the Ninth Amendment to the Loan and Security Agreement. In addition, we are obligated to pay a final payment fee of \$3.2 million at the earlier of the maturity date, acceleration, or payment of the Term Loan.

The Term Loan accrues interest at a floating rate equal to the three-month LIBOR rate (with a floor of 1.00%) plus 7.95% per annum. On March 29, 2020, we and Oxford amended the Loan and Security Agreement to extend the interest-only period. Beginning May 1, 2021, we will be required to make payments of principal and accrued interest in equal monthly installments to amortize the Term Loan through September 1, 2024, the new maturity date.

As security for our obligations under the Loan and Security Agreement, we granted a security interest in substantially all of our existing and after-acquired assets, excluding our intellectual property assets, subject to certain exceptions set forth in the Loan and Security Agreement. If we are unable to discharge these obligations,

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Oxford could foreclose on these assets, which would, at a minimum, have a severe material adverse effect on our ability to operate our business.

Our indebtedness to Oxford could adversely affect our operations and liquidity, by, among other things:

- causing us to use a larger portion of our cash flow to fund interest and principal payments, reducing the availability of cash to fund working capital and capital expenditures and other business activities;
- making it more difficult for us to take advantage of significant business opportunities, such as acquisition opportunities, and to react to changes in market or industry conditions; and
- limiting our ability to borrow additional monies in the future to fund working capital and capital expenditures and for other general corporate purposes.

The Loan and Security Agreement, as amended, requires us to maintain at least \$2.0 million in unrestricted cash and/or cash equivalents and includes certain reporting and other covenants, that, among other things, restrict our ability to (i) dispose of assets, (ii) change the business we conduct, (iii) make acquisitions, (iv) engage in mergers or consolidations, (v) incur additional indebtedness, (vi) create liens on assets, (vii) maintain any collateral account, (viii) pay dividends, (ix) make investments, loans or advances, (x) engage in certain transactions with affiliates, and (xi) prepay certain other indebtedness or amend other financing arrangements. If we fail to comply with any of these covenants or restrictions, such failure may result in an event of default, which if not cured or waived, could result in Oxford causing the outstanding loan amount to become immediately due and payable. If the maturity of our indebtedness is accelerated, we may not have, or be able to timely procure, sufficient cash resources to satisfy our debt obligations, and such acceleration would adversely affect our business and financial condition.

The COVID-19 pandemic has severely impacted the global economic activity and caused significant volatility and negative pressure in the financial markets. This volatility and downturn may affect our business, liquidity position, and financial results. This in turn may negatively impact our ability to remain in compliance with the financial and operating covenants under the Loan and Security Agreement and may restrict our ability to obtain covenant waivers, restructure or amend the terms of our existing debt, or obtain additional debt financing. If the maturity of our indebtedness is accelerated or if we are unable to amend the terms or obtain any necessary waivers under our debt facilities or obtain additional debt or other financing, it would materially and adversely affect our liquidity position and ability to fund our operations. This in turn would materially harm our business and financial conditions.

Our operating results have been and will likely continue to be volatile.

Our prospects must be evaluated in light of the risks and difficulties frequently encountered by emerging companies and particularly by such companies in rapidly evolving and technologically advanced biotech, pharmaceutical and medical device fields. Our visibility as to our future operating results and our clinical development timeline may be further limited by the impact of the ongoing COVID-19 pandemic. In addition, our budgeted expense levels are based in part on our expectations concerning future research and development activities. We may be unable to reduce our expenditures in a timely manner to compensate for any unexpected events. Accordingly, unexpected events could have an immediate and material impact on our business and financial condition. From time to time, we have tried to update our investors' expectations as to our operating results. If we revise any timelines we may give with respect to our clinical trials, it could materially harm our reputation and the market's perception of us and could cause our stock price to decline.

We rely on third parties to conduct our clinical trials, manufacture our product candidates, and perform other services. If these parties are not able to successfully perform due to the impact of the COVID-19 pandemic or otherwise, we may not be able to successfully complete clinical development, obtain regulatory approval or commercialize our product candidates and our business could be substantially harmed.

We rely on third parties in the performance of many of the clinical trial functions, including contract research organizations, that help execute our clinical trials, the hospitals and clinics at which our trials are conducted, the clinical investigators at the trial sites, and other third-party service providers. Failure of any third-party service provider to adhere to applicable trial protocols, laws and regulations in the conduct of one of our clinical trials could adversely affect the conduct and results of such trial (including possible data integrity issues), which could seriously harm our business. The COVID-19 pandemic has placed a strain on hospitals and clinics, contract research organizations, and other providers of clinical and medical supplies and equipment. This in turn could impact the ability of third parties such as hospitals to support our clinical trials or perform other services in support of our clinical programs. In addition, third parties may not prioritize our clinical trials relative to those of other customers due to resource or other constraints as a result of the COVID-19 pandemic. We may experience enrollment at a slower pace at certain of our clinical trial sites than initially anticipated. Further, our clinical trial sites may be required to suspend enrollment due to travel restrictions, workplace safety concerns, quarantine, facility closures, and other governmental restrictions. Some of our clinical trial sites have imposed limited accessibility to conduct clinical monitoring and training on-site. As a result, results from our clinical trials may be delayed, which in turn would have a material adverse impact on our clinical trial plans and timelines and impair our ability to successfully complete clinical development, obtain regulatory approval, or commercialize our product candidates. This in turn would substantially harm our business and operations.

If we experience an interruption in supply from a material sole source supplier, our business may be harmed

We acquire some of our components and other raw materials from sole source suppliers. If there is an interruption in supply of our raw materials from a sole source supplier, for any reason, including due to disruption caused by the COVID-19 pandemic, there can be no assurance that we will be able to obtain adequate quantities of the raw materials within a reasonable time or at commercially reasonable prices. Interruptions in supplies due to pricing, timing, availability, or other issues with our sole source suppliers could have a negative impact on our ability to manufacture products and product candidates, which in turn could adversely affect the development and commercialization of our nanomedicine product candidates and cause us to potentially breach our supply or other obligations under our agreements with certain other counterparties.

We are dependent on sole source suppliers to manufacture the active pharmaceutical ingredients (API) and certain other components of our nanomedicine product candidates. There is no assurance that these sole source suppliers will enter into supply agreements with us to provide contractual assurance to us around supply and pricing. Regardless of whether a sole source supplier enters into a written supply arrangement with us, such supplier could still delay, suspend, or terminate supply of raw materials to us for a number of reasons, including manufacturing or quality issues, payment disputes with us, bankruptcy or insolvency, or other occurrences.

The COVID-19 pandemic has placed a significant strain on the pharmaceutical and medical industries, manufacturers of clinical supplies, and healthcare-related supplies and resources in general. For instance, we have experienced increased difficulties in obtaining certain materials for manufacturing that are also components of COVID-19 vaccine candidates. The impact of the COVID-19 pandemic has exacerbated the risks to which we are subject due to our reliance on third-party (and in some cases, sole source) suppliers. Additionally, our suppliers may experience operational difficulties, and resource constraints due to the impact of the COVID-19 pandemic. If our third-party suppliers were to encounter any of these difficulties, or otherwise fail to comply with their contractual obligations, our ability to provide our product candidates to patients in clinical trials would be jeopardized. Any delay or interruption in the procurement of clinical trial supplies could delay the completion of clinical trials, increase the costs associated with maintaining clinical trial programs and, depending upon the period of delay, require us to commence new clinical trials at additional expense or terminate clinical trials completely.

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If a sole source supplier ceases supply of raw materials necessary there is no guarantee that we will find an alternative supplier for the necessary raw materials on terms acceptable to us, or at all. Further the qualification process for a new vendor could take months or years, and any such day in qualification could significantly harm our business.

If we are unable to identify, hire and/or retain key personnel, or if any of our personnel were to test positive for COVID-19, we may not be able to sustain or grow our business.

We maintain a very small executive team. Our ability to operate successfully and manage our potential future growth depends significantly upon our ability to attract, retain, and motivate highly skilled and qualified research, technical, clinical, regulatory, sales, marketing, managerial and financial personnel. We compete for talent with numerous companies, as well as universities and non-profit research organizations. In the future, we may hire a significant number of scientists, quality and regulatory personnel, and other technical staff with the requisite expertise to support and expand our nanomedicine business. The manufacturing of our oncology drug assets is a highly complex process that requires significant experience and know-how. If we are unable to attract personnel with the necessary skills and experience to reestablish and expand our nanomedicine business, which is currently conducted out of our San Antonio, Texas facility, our business could suffer.

Our future success also depends on the personal efforts and abilities of the principal members of our senior management and scientific staff to provide strategic direction, manage our operations, and maintain a cohesive and stable environment. In particular, we are highly dependent on our executive officers, especially Marc Hedrick, M.D., our Chief Executive Officer. Given his leadership, extensive technical, scientific, and financial expertise and management and operational experience, if we were unable to retain the services of Dr. Hedrick for any reason, it would materially and adversely impact our business and operations. Further, the loss of services of Dr. Hedrick or any other executive officer could result in product development delays or the failure of our collaborations with current and future collaborators, which, in turn, may hurt our ability to develop and commercialize products and generate revenue. We do not maintain key man life insurance on the lives of any of the members of our senior management. The loss of key personnel for any reason or our inability to hire, retain, and motivate additional qualified personnel in the future could prevent us from sustaining or growing our business. In addition, if any of our personnel were to test positive for COVID-19, it would likely significantly impair our operations. The loss of services of any of our personnel, including Dr. Hedrick, particularly for an extended period due to COVID-19 or otherwise, would likely result in product development delays or the failure of our collaborations with current and future collaborators, which, in turn, may impede or delay our ability to develop and commercialize products and generate revenue. In addition, it could also result in difficulty to obtain additional funding for our development of products and our future operations.

Risks Related to Our Common Stock

Our stockholders may experience substantial dilution in the value of their investment if we issue additional shares of our capital stock, including in connection with the sale or issuance of our common stock to Lincoln Park, the sale of the shares of common stock acquired by Lincoln Park, and the sale of our common stock by Canaccord. Further, sales of our common stock, or the perception that such sales may occur, could cause the price of our common stock to decline.

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. 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. 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

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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.

We also may issue and sell, from time to time, shares of our common stock having an aggregate offering price of up to \$10,000,000, depending on market demand, with Canaccord acting as an agent for sales. Sales of the ATM Shares may be made by any method permitted by law deemed to be an “at the market offering” as defined in Rule 415(a)(4) of the Securities Act, including, without limitation, sales made directly on or through the Nasdaq Capital Market. Canaccord will use its commercially reasonable efforts to sell the ATM Shares we request to be sold on our behalf, consistent with Canaccord’s normal trading and sales practices, under the terms and subject to the conditions set forth in the Distribution Agreement. We have no obligation to sell any of the ATM Shares. We may instruct Canaccord not to sell the ATM Shares if the sales cannot be effected at or above the price we designate from time to time and we may at any time suspend sales pursuant to the Distribution Agreement.

Our charter allows us to issue up to 100,000,000 shares of our common stock and to issue and designate the rights of, without stockholder approval, up to 5,000,000 shares of preferred stock. We will need to raise additional capital in order to initiate or complete additional development activities for all of our product candidates, to pursue additional disease indications for our product candidates, or to finance future strategic investments or acquisitions. This in turn may require us to issue a substantial amount of securities. As a result, we may in the future sell additional shares of our common stock or other securities convertible into or exchangeable for our common stock, including at prices that may be lower than the prices paid by existing stockholders, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders, which could result in substantial dilution to the interests of existing stockholders. There can be no assurance that we 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. 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. See the “Dilution” section in this prospectus for a description of shares of common stock we have sold and issued pursuant to our ATM facility and equity line program and the exercise of warrants subsequent to December 31, 2020. 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. 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.

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

The market price of our common stock has been, and may continue to be, subject to significant fluctuations. Among the factors that may cause the market price of our common stock to fluctuate are the risks described in this “Risk Factors” section and other factors, including:

- fluctuations in our operating results or the operating results of our competitors;
- the outcome of clinical trials involving the use of our products, including our sponsored trials;
- changes in estimates of our financial results or recommendations by securities analysts;
- variance in our financial performance from the expectations of securities analysts;
- changes in the estimates of the future size and growth rate of our markets;

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- changes in accounting principles or changes in interpretations of existing principles, which could affect our financial results;
- conditions and trends in the markets we currently serve or which we intend to target with our product candidates;
- changes in general economic, industry and market conditions;
- the impact of short selling or the impact of a potential “short squeeze” resulting from a sudden increase in demand for our stock;
- the impact of the COVID-19 impact, including the magnitude, severity, duration, and uncertainty of the downturn in the domestic and global economies and financial markets;
- success of competitive products and services;
- changes in market valuations or earnings of our competitors;
- announcements of significant new products, contracts, acquisitions or strategic alliances by us or our competitors;
- our continuing ability to list our securities on an established market or exchange;
- the timing and outcome of regulatory reviews and approvals of our products;
- the commencement or outcome of litigation involving our company, our general industry or both;
- changes in our capital structure, such as future issuances of securities or the incurrence of additional debt;
- actual or expected sales of our common stock by the holders of our common stock; and
- the trading volume of our common stock.

In addition, the financial markets may experience a loss of investor confidence or otherwise experience continued volatility and deterioration due to the COVID-19 pandemic. A loss of investor confidence may result in extreme price and volume fluctuations in our common stock that are unrelated or disproportionate to the operating performance of our business, our financial condition or results of operations, which may materially harm the market price of our common stock and result in substantial losses for stockholders. Further, although our common stock is traded on the Nasdaq Capital Market, there is currently a limited market for our common stock and an active market may never develop. An active trading market in our common stock may not develop.

We may be or become the target of securities litigation, which is costly and time-consuming to defend.

In the past, following periods of market volatility in the price of a company’s securities, the reporting of unfavorable news or continued decline in a company’s stock price, security holders have often instituted class action litigation. The market value of our securities has steadily declined over the past several years for a variety of reasons discussed elsewhere in this “Risk Factors” section, which heightens our litigation risk. If we face such litigation, we could incur substantial legal costs and our management’s attention could be diverted from the operation of our business, causing our business to suffer. Any adverse determination in any such litigation or any amounts paid to settle any such actual or threatened litigation could require that we make significant payments.

We may issue debt and equity securities or securities convertible into equity securities, any of which may be senior to our common stock as to distributions and in liquidation, which could negatively affect the value of our common stock.

In the future, we may attempt to increase our capital resources by entering into debt or debt-like financing that is unsecured or secured by up to all of our assets, or by issuing additional debt or equity securities, which

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could include issuances of secured or unsecured commercial paper, medium-term notes, senior notes, subordinated notes, guarantees, preferred stock, hybrid securities, or securities convertible into or exchangeable for equity securities. In the event of our liquidation, our lenders and holders of our debt and preferred securities would receive distributions of our available assets before distributions to the holders of our common stock. Because our decision to incur debt and issue securities in future offerings may be influenced by market conditions and other factors beyond our control, we cannot predict or estimate the amount, timing or nature of our future offerings or debt financings. Further, market conditions could require us to accept less favorable terms for the issuance of our securities in the future.

We could be delisted from Nasdaq, which would seriously harm the liquidity of our stock and our ability to raise capital.

The Nasdaq Stock Market has experienced significant volatility due to the COVID-19 pandemic, which has also impacted our stock price. In addition, we have a limited public float and our stock price has experienced a significant decline since our corporate restructuring in 2019. Between January 1, 2020 and December 31, 2020, our closing stock price has fluctuated from a high of \$3.14 at September 16, 2020 to a low of \$1.05 at March 23, 2020.

On August 19, 2019, we received a written notice from Nasdaq staff indicating that we no longer met the alternative compliance standards of market value of listed securities or net income from continuing operations for continued listing on the Nasdaq Capital Market under Nasdaq Listing Rule 5550(b)(1) (the “Nasdaq Rule”). On August 12, 2020, we received a written notice from Nasdaq that we had regained compliance with the Nasdaq Rule. Based on our stockholders’ equity of \$3.1 million as of December 31, 2020, we continue to meet the minimum stockholders’ equity requirement for continued listing on the Nasdaq Capital Market under the Nasdaq Rule. However, if we fail to meet such requirement in the future, there is a risk that our common stock may be delisted from Nasdaq, which would adversely impact liquidity of our common stock and potentially result in even lower bid prices for our common stock.

If, for any reason, Nasdaq were to delist our securities from trading on its exchange and we are unable to obtain listing on another reputable national securities exchange, a reduction in some or all of the following may occur, each of which could materially adversely affect our stockholders:

- the liquidity and marketability of our common stock;
- the market price of our common stock;
- our ability to obtain financing for the continuation of our operations;
- the number of institutional and general investors that will consider investing in our common stock;
- the number of market makers in our common stock;
- the availability of information concerning the trading prices and volume of our common stock; and
- the number of broker-dealers willing to execute trades in shares of our common stock.

FORWARD-LOOKING STATEMENTS

This prospectus 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 this prospectus under “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, both of which are 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;
- market conditions;
- the progress, scope or duration of the development of product candidates or programs;

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- 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 to Lincoln Park.

We encourage you to read these risks carefully. We caution you not to place undue reliance on the forward-looking statements contained or incorporated by reference in this prospectus. 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 SEC.

THE LINCOLN PARK TRANSACTION

General

On September 30, 2020, we entered into the Purchase Agreement with Lincoln Park, pursuant to which Lincoln Park has agreed to purchase from us up to an aggregate of \$25.0 million of our common stock (subject to certain limitations) from time to time over the term of the Purchase Agreement. Also on September 30, 2020, we entered into the Registration Rights Agreement pursuant to which we filed with the SEC the registration statement that includes this prospectus to register for resale under the Securities Act the shares of our common stock that may be issued to Lincoln Park under the Purchase Agreement.

We previously filed the Prior Registration Statement covering the resale by the selling stockholder of up to 1,519,000 shares of our common stock, comprised of: (i) 180,701 Commitment Shares that we issued to Lincoln Park on October 2, 2020 and (ii) up to an additional 1,338,299 shares of our common stock that we had reserved for issuance and sale to Lincoln Park under the Purchase Agreement from time to time from and after the Commencement Date. From the Commencement Date through February 11, 2021, we sold an aggregate of 1,338,299 shares of our common stock to Lincoln Park under the Purchase Agreement, exhausting all of the shares of common stock that were previously registered for resale by Lincoln Park on the Prior Registration Statement. This prospectus covers the resale of up to an additional 4,500,000 shares of our common stock that we have reserved for issuance and sale to Lincoln Park under the Purchase Agreement from time to time from and after the date of this prospectus, if and when we determine to sell additional shares of our common stock to Lincoln Park under the Purchase Agreement.

Other than the 180,701 Commitment Shares that we issued to Lincoln Park as a fee for making its irrevocable commitment to purchase our common stock under the Purchase Agreement, we did not have the right to commence sales of our common stock to Lincoln Park under the Purchase Agreement until the Commencement Date. From and after the Commencement Date, we may, from time to time and at our sole discretion for a period of 36 months after the Commencement Date, on any business day that we select on which the closing sale price of our common stock equals or exceeds \$0.25 per share, direct Lincoln Park to purchase in a Regular Purchase up to 50,000 shares of our common stock, which amount may be increased depending on the market price of our common stock at the time of sale, subject to a maximum commitment of \$500,000 per Regular Purchase. In addition, at our discretion, Lincoln Park has committed to purchase other “accelerated amounts” and/or “additional accelerated amounts” under certain circumstances. We will control the timing and amount of any sales of our common stock to Lincoln Park. The purchase price of the shares of our common stock that have been sold and may be sold to Lincoln Park in Regular Purchases under the Purchase Agreement was and will be based on the market price of our common stock preceding the time of sale as computed under the Purchase Agreement. The purchase price per share will be equitably adjusted as provided in the Purchase Agreement for any reorganization, recapitalization, non-cash dividend, stock split, or other similar transaction as set forth in the Purchase Agreement. We may at any time in our sole discretion terminate the Purchase Agreement without fee, penalty or cost upon one business day notice. There are no restrictions on future financings, rights of first refusal, participation rights, penalties or liquidated damages in the Purchase Agreement or Registration Rights Agreement, other than a prohibition on our entering into certain types of transactions that are defined in the Purchase Agreement as “Variable Rate Transactions.” Lincoln Park may not assign or transfer its rights and obligations under the Purchase Agreement.

As of February 24, 2021, there were 9,166,902 shares of our common stock outstanding, of which 9,129,988 shares of our common stock were held by non-affiliates. The 9,166,902 shares of our common stock outstanding as of February 24, 2021 includes 1,338,299 shares previously issued and sold to Lincoln Park under the Purchase Agreement. If all of the 4,500,000 shares offered by Lincoln Park under this prospectus were issued and outstanding, such shares would represent approximately 32.9% of the total number of shares of our common stock outstanding and approximately 33.0% of the total number of outstanding shares held by non-affiliates, in each case as of February 24, 2021. The Purchase Agreement provides that we may sell up to an aggregate of

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\$25.0 million of our common stock to Lincoln Park. As of February 11, 2021, we have sold an aggregate of 1,338,299 shares of our common stock to Lincoln Park under the Purchase Agreement for an aggregate of approximately \$3.6 million, all of which shares were registered for resale on the Prior Registration Statement. Since we have previously issued and sold to Lincoln Park all of the shares of common stock that were registered for resale by Lincoln Park on the Prior Registration Statement, we have filed the registration statement that includes this prospectus so that we may issue and sell to Lincoln Park up to an additional 4,500,000 shares of our common stock from time to time from and after the date of this prospectus. Depending on the market prices of our common stock at the time we elect to issue and sell such additional shares to Lincoln Park under the Purchase Agreement, we may need to sell more shares to Lincoln Park than are offered under this prospectus to receive aggregate gross proceeds equal to the \$21.4 million balance of the \$25.0 million total commitment available to us under the Purchase Agreement, in which case we must first register for resale under the Securities Act additional shares of our common stock, which could cause additional substantial dilution to our stockholders. The number of shares ultimately offered for resale by Lincoln Park is dependent upon the number of shares we sell to Lincoln Park under the Purchase Agreement.

Under applicable Nasdaq rules, in no event may we issue or sell to Lincoln Park under the Purchase Agreement shares of our common stock in excess of the Exchange Cap of 917,823 shares (including the 180,701 Commitment Shares), which represents 19.99% of the shares of our common stock outstanding (based on 4,591,415 shares outstanding) immediately prior to the execution of the Purchase Agreement, unless (i) we obtain stockholder approval to issue shares of our common stock in excess of the Exchange Cap or (ii) the average price of all applicable sales of our common stock to Lincoln Park under the Purchase Agreement equals or exceeds \$3.1872 per share (which represents the lower of (A) the official closing price of our common stock on Nasdaq on the trading day immediately preceding the date of the Purchase Agreement and (B) the average official closing price of our common stock on Nasdaq for the five consecutive trading days ending on the trading day immediately preceding the date of the Purchase Agreement, plus an incremental amount of \$0.6272 attributable to the value of the Commitment Shares), so that such issuances and sales would be exempt from the Exchange Cap limitation under applicable Nasdaq rules. In any event, the Purchase Agreement specifically provides that we may not issue or sell any shares of our common stock under the Purchase Agreement if such issuance or sale would breach any applicable rules or regulations of The Nasdaq Stock Market.

Prior to entering into the Purchase Agreement with Lincoln Park, on June 16, 2020, we received stockholder approval pursuant to Nasdaq Listing Rules 5635(a), 5635(b) and 5635(d) to permit issuances of our common stock (including the issuance of more than 19.99% of our common stock) to Lincoln Park pursuant to the Purchase Agreement. Based on the closing price of our common stock of \$1.05 per share on March 16, 2020 (the lowest closing sale price since January 1, 2020 as reported on Nasdaq.com), the maximum number of shares we can issue and sell to Lincoln Park under the Purchase Agreement is approximately 23.8 million shares. Accordingly, we requested and received stockholder approval for the issuance of up to 23.8 million shares of our common stock under the Purchase Agreement. We would seek additional stockholder approval before issuing more than 23.8 million shares under the Purchase Agreement.

The Purchase Agreement also prohibits us from directing Lincoln Park to purchase any shares of common stock if those shares, when aggregated with all other shares then beneficially owned by Lincoln Park and its affiliates, would result in Lincoln Park having beneficial ownership of shares of our common stock, as calculated pursuant to Section 13(d) of the Exchange Act and Rule 13d-3 thereunder, in excess of the Beneficial Ownership Cap at any time.

There are substantial risks to our stockholders as a result of the sale and issuance of common stock to Lincoln Park under the Purchase Agreement. These risks include substantial dilution, significant declines in our stock price and our inability to draw sufficient funds when needed. See “Risk Factors.” The sale of our common stock to Lincoln Park under the Purchase Agreement will not affect the rights or privileges of our other stockholders, except that the economic and voting interests of our existing stockholders will be diluted as a result of any such sale. Although the number of shares of common stock that our other stockholders own will not

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decrease, the shares of our common stock owned by our other stockholders will represent a smaller percentage of our total outstanding shares after any such sale to Lincoln Park under the Purchase Agreement.

Purchase of Shares of our Common Stock under the Purchase Agreement

Under the Purchase Agreement, we may from time to time, at our discretion, direct Lincoln Park to purchase up to 50,000 shares of our common stock in a Regular Purchase on such business day, provided, however, that the Regular Purchase may be increased to up to 100,000 shares of our common stock, provided that the closing sale price of our common stock is not below \$2.50 on the purchase date (such share amount limitation, the "Regular Purchase Share Limit"). In each case, Lincoln Park's maximum commitment in any single Regular Purchase may not exceed \$500,000. The Regular Purchase Share Limit is subject to proportionate adjustment in the event of a reorganization, recapitalization, non-cash dividend, stock split or other similar transaction; provided, that if after giving effect to such full proportionate adjustment, the adjusted Regular Purchase Share Limit would preclude us from requiring Lincoln Park to purchase shares of our common stock at an aggregate purchase price equal to or greater than \$150,000 in any single Regular Purchase, then the Regular Purchase Share Limit will not be fully adjusted, but rather the Regular Purchase Share Limit for such Regular Purchase shall be adjusted as specified in the Purchase Agreement, such that, after giving effect to such adjustment, the Regular Purchase Share Limit will be equal to (or as close as can be derived from such adjustment without exceeding) \$150,000.

The purchase price per share for each such Regular Purchase will be equal to the lower of:

- the lowest sale price for our common stock on the purchase date for such shares of our common stock; and
- the arithmetic average of the three lowest closing sale prices for our common stock during the 10 consecutive business days ending on the business day immediately preceding the purchase date of such shares of our common stock.

In addition to Regular Purchases described above, we may also direct Lincoln Park, on any business day on which we have properly submitted a Regular Purchase notice directing Lincoln Park to purchase the maximum number of shares of our common stock that we are then permitted to include in a single Regular Purchase notice, to purchase an additional amount of our common stock, which we refer to as an Accelerated Purchase, not to exceed the lesser of:

- 30% of the aggregate number of shares of our common stock traded during all or, if certain trading volume or market price thresholds specified in the Purchase Agreement are crossed on the applicable Accelerated Purchase date, which is defined as the next business day following the purchase date for the corresponding Regular Purchase, the portion of the normal trading hours on the applicable Accelerated Purchase date prior to such time that any one of such thresholds is crossed, which period of time on the applicable Accelerated Purchase date we refer to as the Accelerated Purchase Measurement Period; and
- 300% of the number of purchase shares purchased pursuant to the corresponding Regular Purchase.

The purchase price per share for each such Accelerated Purchase will be equal to 96.5% of the lower of:

- the volume weighted average price of our common stock during the Accelerated Purchase Measurement Period on the applicable Accelerated Purchase date; and
- the closing sale price of our common stock on the applicable Accelerated Purchase date.

We may also direct Lincoln Park, not later than 1:00 p.m., Eastern time, on a business day on which an Accelerated Purchase has been completed and all of the shares of our common stock to be purchased thereunder (and under the corresponding Regular Purchase) have been properly delivered to Lincoln Park in accordance with

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the Purchase Agreement prior to such time on such business day, to purchase an additional amount of our common stock, which we refer to as an Additional Accelerated Purchase, of up to the lesser of:

- 30% of the aggregate number of shares of our common stock traded during a certain portion of the normal trading hours on such Accelerated Purchase date as determined in accordance with the Purchase Agreement, which period of time we refer to as the Additional Accelerated Purchase Measurement Period; and
- 300% of the number of purchase shares purchased pursuant to the Regular Purchase corresponding to the Accelerated Purchase that was completed on such Accelerated Purchase date on which an Additional Accelerated Purchase notice was properly received.

We may, in our sole discretion, submit multiple Additional Accelerated Purchase notices to Lincoln Park prior to 1:00 p.m., Eastern time, on a single Accelerated Purchase date, provided that all prior Accelerated Purchases and Additional Accelerated Purchases (including those that have occurred earlier on the same day) have been completed and all of the shares of our common stock to be purchased thereunder (and under the corresponding Regular Purchase) have been properly delivered to Lincoln Park in accordance with the Purchase Agreement.

The purchase price per share for each such Additional Accelerated Purchase will be equal to 95% of the lower of:

- the volume weighted average price of our common stock during the applicable Additional Accelerated Purchase Measurement Period on the applicable Additional Accelerated Purchase date; and
- the closing sale price of our common stock on the applicable Additional Accelerated Purchase date.

In the case of Regular Purchases, Accelerated Purchases and Additional Accelerated Purchases, the purchase price per share will be equitably adjusted for any reorganization, recapitalization, non-cash dividend, stock split, reverse stock split or other similar transaction occurring during the business days used to compute the purchase price.

Other than as described above, there are no trading volume requirements or restrictions under the Purchase Agreement, and we will control the timing and amount of any sales of our common stock to Lincoln Park.

Minimum Share Price

Under the Purchase Agreement, we and Lincoln Park may not effect any sales of shares of our common stock under the Purchase Agreement on any purchase date that the closing sale price of our common stock is less than the floor price of \$0.25 per share of common stock, which will be appropriately adjusted for any reorganization, recapitalization, non-cash dividend, stock split or other similar transaction. Upon consummation of any such reorganization, recapitalization, non-cash dividend, stock split or other similar transaction, the adjusted floor price per share of common stock will be the lower of (i) the adjusted price and (ii) \$1.00.

Events of Default

Events of default under the Purchase Agreement include the following:

- the effectiveness of the registration statement of which this prospectus forms a part lapses for any reason (including, without limitation, the issuance of a stop order), or any required prospectus supplement and accompanying prospectus are unavailable for the resale by Lincoln Park of our common stock offered hereby, and such lapse or unavailability continues for a period of 10 consecutive business days or for more than an aggregate of 30 business days in any 365-day period;
- suspension by our principal market of our common stock from trading for a period of one business day;

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- the de-listing of our common stock from the Nasdaq Capital Market, our principal market, provided our common stock is not immediately thereafter trading on the New York Stock Exchange, the Nasdaq Capital Market, the Nasdaq Global Market, the Nasdaq Global Select Market, the NYSE American, the NYSE Arca, or the OTCQX Best Market or the OTCQB Venture Market operated by OTC Markets Group Inc. (or nationally recognized successor thereto);
- the failure of our transfer agent to issue to Lincoln Park shares of our common stock within two business days after the applicable date on which Lincoln Park is entitled to receive such shares of our common stock;
- any breach of the representations or warranties or covenants contained in the Purchase Agreement or Registration Rights Agreement that has or could have a material adverse effect on us and, in the case of a breach of a covenant that is reasonably curable, that is not cured within five business days;
- any voluntary or involuntary participation or threatened participation in insolvency or bankruptcy proceedings by or against us;
- if at any time we are not eligible to transfer our common stock electronically; or
- if at any time the Exchange Cap (to the extent applicable under the terms of the Purchase Agreement) is reached and our stockholders have not approved the issuance of common stock in excess of the Exchange Cap in accordance with applicable Nasdaq rules.

Lincoln Park does not have the right to terminate the Purchase Agreement upon any of the events of default set forth above, although the Purchase Agreement would automatically terminate in the event of any voluntary or involuntary participation or threatened participation in insolvency or bankruptcy proceedings by or against us. During an event of default, all of which are outside of Lincoln Park's control, we may not direct Lincoln Park to purchase any shares of our common stock under the Purchase Agreement.

Our Termination Rights

We have the unconditional right, at any time, for any reason and without any payment or liability to us, to give notice to Lincoln Park to terminate the Purchase Agreement.

No Short-Selling or Hedging by Lincoln Park

Lincoln Park has agreed that neither it nor any of its affiliates shall engage in any direct or indirect short-selling or hedging of our common stock during any time prior to the termination of the Purchase Agreement.

Prohibitions on Variable Rate Transactions

There are no restrictions on future financings, rights of first refusal, participation rights, penalties or liquidated damages in the Purchase Agreement or Registration Rights Agreement other than a prohibition on entering into a "Variable Rate Transaction," as defined in the Purchase Agreement.

Effect of Performance of the Purchase Agreement on Our Stockholders

All 4,500,000 shares of our common stock being registered for resale in this offering that may be issued or sold by us to Lincoln Park under the Purchase Agreement are expected to be freely tradable. It is anticipated that shares registered for resale in this offering will be sold at our sole discretion from time to time from and after the date of this prospectus for a period of 36 months after the Commencement Date. The sale by Lincoln Park of a significant amount of shares of our common stock registered in this offering at any given time could cause the market price of our common stock to decline and to be highly volatile. Sales of our common stock to Lincoln Park, if any, will depend upon market conditions and other factors to be determined by us. We may ultimately

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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 additional shares of our common stock to Lincoln Park, after Lincoln Park has acquired the shares of our common stock, Lincoln Park may resell all, some or none of those additional shares of our common stock at any time or from time to time in its discretion. Therefore, additional sales to Lincoln Park by us under the Purchase Agreement may result in substantial dilution to the interests of other holders of our common stock. In addition, if we sell a substantial number of shares of our common stock to Lincoln Park under the Purchase Agreement, or if investors expect that we will do so, the actual sales of shares of our common stock or the mere existence of our arrangement with Lincoln Park may 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 such sales. However, we have the right to control the timing and amount of any additional sales of our common stock to Lincoln Park and the Purchase Agreement may be terminated by us at any time at our discretion without any cost to us.

Pursuant to the terms of the Purchase Agreement, we have the right, but not the obligation, from time to time to direct Lincoln Park to purchase up to \$25.0 million of our common stock (exclusive of the 180,701 Commitment Shares issued to Lincoln Park). Depending on the price per share at which we sell our common stock to Lincoln Park pursuant to the Purchase Agreement, we may need to sell to Lincoln Park more shares of our common stock than are offered under this prospectus in order to receive aggregate gross proceeds equal to the \$21.4 million balance of the \$25.0 million total commitment available to us under the Purchase Agreement. If we choose to do so, we must first register for resale under the Securities Act such additional shares of our common stock, which could cause additional substantial dilution to our stockholders. The number of shares ultimately offered for resale by Lincoln Park under this prospectus is dependent upon the number of shares we direct Lincoln Park to purchase under the Purchase Agreement.

The Purchase Agreement prohibits us from issuing or selling to Lincoln Park under the Purchase Agreement (i) shares of our common stock in excess of the Exchange Cap, unless we obtain stockholder approval to issue shares in excess of the Exchange Cap or the average price of all applicable sales of our common stock to Lincoln Park under the Purchase Agreement equals or exceeds \$3.1872 per share (which represents the lower of (A) the official closing price of our common stock on Nasdaq on the trading day immediately preceding the date of the Purchase Agreement and (B) the average official closing price of our common stock on Nasdaq for the five consecutive trading days ending on the trading day immediately preceding the date of the Purchase Agreement, plus an incremental amount of \$0.6272 attributable to the value of the Commitment shares), such that the transactions contemplated by the Purchase Agreement are exempt from the Exchange Cap limitation under applicable Nasdaq rules and (ii) any shares of our common stock if those shares, when aggregated with all other shares of our common stock then beneficially owned by Lincoln Park, would exceed the Beneficial Ownership Cap. Prior to entering into the Purchase Agreement with Lincoln Park, on June 16, 2020, we received stockholder approval pursuant to Nasdaq Listing Rules 5635(a), 5635(b), and 5635(d) to permit issuances of a maximum of up to 23.8 million shares of our common stock in the aggregate (or approximately 22.9 million shares in excess of the Exchange Cap) to Lincoln Park pursuant to the Purchase Agreement.

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As of February 11, 2021, we have sold an aggregate of 1,338,299 shares of our common stock to Lincoln Park under the Purchase Agreement for an aggregate of approximately \$3.6 million, all of which shares (together with the 180,701 Commitment Shares) were registered for resale on the Prior Registration Statement. Since we have previously issued and sold to Lincoln Park all of the shares of common stock that were registered for resale by Lincoln Park on the Prior Registration Statement, we have filed the registration statement that includes this prospectus so that we may issue and sell to Lincoln Park up to an additional 4,500,000 shares of our common stock from time to time from and after the date of this prospectus. The following table sets forth the amount of gross proceeds we may receive from Lincoln Park from our sale of up to 4,500,000 shares of our common stock that we may issue and sell to Lincoln Park in the future under the Purchase Agreement at varying purchase prices from time to time from and after the date of this prospectus:

<u>Assumed Average Purchase Price Per Share</u>	<u>Number of to be Issued if Full Purchase(1)</u>	<u>Percentage of Outstanding Shares of Common Stock After Giving Effect to the Sales to Lincoln Park(2)</u>	<u>Gross Proceeds from the Future Sale of Shares to Lincoln Park Under the Purchase Agreement(1)</u>
\$1.00	4,500,000	32.9%	\$ 4,500,000
\$2.00	4,500,000	32.9%	\$ 9,000,000
\$3.00	4,500,000	32.9%	\$ 13,500,000
\$3.08(3)	4,500,000	32.9%	\$ 13,860,000
\$4.00	4,500,000	32.9%	\$ 18,000,000

- (1) Although the Purchase Agreement provides that we may sell up to \$25.0 million of our common stock to Lincoln Park, we are only registering 4,500,000 shares of our common stock for resale under the registration statement of which this prospectus is a part, which, together with the 1,338,299 shares of our common stock registered for resale under the Prior Registration Statement (excluding the 180,701 Commitment Shares), may or may not cover all the shares of our common stock we ultimately sell to Lincoln Park under the Purchase Agreement, depending on the purchase price per share.
- (2) The denominator is based on 9,166,902 shares of our common stock outstanding as of February 24, 2021, adjusted to include the number of shares set forth in the adjacent column which we would have sold to Lincoln Park, assuming the purchase price in the adjacent column. The numerator is based on the number of shares issuable under the Purchase Agreement at the corresponding assumed purchase price set forth in the adjacent column, without giving effect to the Beneficial Ownership Cap.
- (3) The closing sale price per share of our common stock on February 24, 2021.

USE OF PROCEEDS

This prospectus relates to shares of our common stock that may be offered and sold from time to time by Lincoln Park. We will receive no proceeds from the sale of shares of common stock by Lincoln Park in this offering. We may receive up to \$25.0 million in aggregate gross proceeds under the Purchase Agreement from any sales we make to Lincoln Park pursuant to the Purchase Agreement. We estimate that the net proceeds to us from the sale of our common stock to Lincoln Park pursuant to the Purchase Agreement would be up to \$24.7 million over a period of approximately 36 months after the Commencement Date, assuming that we sell the full amount of our common stock that we have the right, but not the obligation, to sell to Lincoln Park under the Purchase Agreement, and after estimated fees and expenses.

As of February 11, 2021, we received approximately \$3.6 million in aggregate proceeds from the sale of shares of our common stock to Lincoln Park under the Purchase Agreement, leaving a balance of approximately \$21.4 million of the \$25.0 million total commitment of Lincoln Park under the Purchase Agreement. Assuming a purchase price of \$3.08 (which represents the closing price of our common stock on February 24, 2021), the purchase by Lincoln Park of the entire 4,500,000 additional shares being registered for resale hereunder would result in gross proceeds to us of approximately \$13.9 million, which together with the \$3.6 million we sold to Lincoln Park under the Purchase Agreement between the Commencement Date and February 11, 2021, would result in total gross proceeds to us of \$17.5 million of the \$25.0 million total commitment under the Purchase Agreement. See “Plan of Distribution” elsewhere in this prospectus for more information.

We expect to use any proceeds that we receive under the Purchase Agreement for working capital and general corporate purposes. 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 we are unable to predict the timing or amount of potential issuances of all of the additional shares issuable to the Purchase Agreement, we cannot specify with certainty all of the particular uses for the net proceeds that we will have from the sale of such additional shares. Accordingly, our management will have broad discretion in the application of the net proceeds. We may also use a portion of the net proceeds 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. We may use the proceeds for purposes that are not contemplated at the time of this offering. 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. It is possible that no additional shares will be issued under the Purchase Agreement. It is possible that no additional shares will be issued to Lincoln Park under the Purchase Agreement.

DILUTION

The sale of our common stock to Lincoln Park pursuant to the Purchase Agreement will have a dilutive impact on our stockholders. In addition, the lower our stock price is at the time we exercise our right to sell shares to Lincoln Park, the more shares of our common stock we will have to issue to Lincoln Park pursuant to the Purchase Agreement and our existing stockholders would experience greater dilution.

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.

Through the date of this prospectus, we have sold approximately \$3.6 million of our common stock to Lincoln Park under the Purchase Agreement, leaving an approximately \$21.4 million balance of the \$25.0 million total commitment of Lincoln Park under the Purchase Agreement.

After giving effect to the assumed sale of 4,500,000 shares of our common stock to Lincoln Park pursuant to the Purchase Agreement at an assumed sale price of \$3.08 per share of our common stock (which represents the closing price of our common stock on February 24, 2021) and after deducting estimated offering expenses payable by us, our as-adjusted net tangible book value as of December 31, 2020 would have been approximately \$16.3 million, or \$1.45 per share. This represents an immediate increase in net tangible book value of \$1.07 per share to existing stockholders and an immediate dilution of \$1.63 per share to new investors. The table below illustrates this per share dilution:

Assumed offering price per share		\$3.08
Historical net tangible book value per share as of December 31, 2020	\$0.38	
Increase per share attributable to this offering	<u>\$1.07</u>	
As adjusted net tangible book value per share after this offering		<u>\$1.45</u>
Dilution per share to new investors		<u>\$1.63</u>

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 under our equity incentive plans, with a weighted-average exercise price of \$10.01 per share;
- 210,389 shares of common stock reserved for future issuance under our 2015 New Employee Incentive Plan; and
- 159,939 shares of common stock reserved for future issuance under our 2020 Stock 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; and
- 3,113,625 shares of common stock issuable upon the exercise of warrants to purchase common stock, with a weighted-average exercise price of \$2.62 per share.

During 2021 and through the date of this prospectus, we issued and sold 985,186 shares of our common stock under the Purchase Agreement for net proceeds of \$2.9 million, and issued 536,070 shares under the Distribution Agreement for net proceeds of \$1.5 million. In February 2021, certain warrant holders exercised warrants to purchase 896,500 shares of our common stock for total exercise proceeds of \$2.0 million. 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, it could result in further dilution to our stockholders.

SELLING STOCKHOLDER

This prospectus relates to the possible resale by the selling stockholder, Lincoln Park, of shares of our common stock that may be issued to Lincoln Park pursuant to the Purchase Agreement. We are filing the registration statement that includes this prospectus pursuant to the provisions of the Registration Rights Agreement, which we entered into with Lincoln Park on September 30, 2020, concurrently with our execution of the Purchase Agreement, in which we agreed to provide certain registration rights with respect to sales by Lincoln Park of the shares of our common stock that may be issued to Lincoln Park under the Purchase Agreement.

Lincoln Park, as the selling stockholder, may, from time to time, offer and sell pursuant to this prospectus any or all of the shares of our common stock that we may sell to Lincoln Park from time to time at our discretion under the Purchase Agreement. The selling stockholder may sell some, all, or none of its shares. We do not know how long the selling stockholder will hold the shares before selling them, and we currently have no agreements, arrangements or understandings with the selling stockholder regarding the sale of any of the shares.

The following table presents information regarding the selling stockholder and the shares of our common stock that it may offer and sell from time to time under this prospectus. The table is prepared based on information supplied to us by the selling stockholder, and reflects its holdings as of February 24, 2021. Neither Lincoln Park nor any of its affiliates has held a position or office, or had any other material relationship, with us or any of our predecessors or affiliates. Beneficial ownership is determined in accordance with Section 13(d) of the Exchange Act and Rule 13d-3 thereunder. The percentage of shares of our common stock beneficially owned prior to the offering is based on 9,166,902 shares of our common stock outstanding as of February 24, 2021.

Name	Shares of our Common Stock Beneficially Owned Prior to Offering ⁽¹⁾⁽²⁾		Number of Shares of Common Stock Being Offered	Shares of our Common Stock Beneficially Owned After Offering ⁽³⁾⁽⁴⁾⁽⁵⁾	
	Number	%		Number	%
Lincoln Park Capital Fund, LLC ⁽⁶⁾	—	—	4,500,000	4,500,000	32.9%

- (1) We have excluded from the number of shares beneficially owned by Lincoln Park prior to the offering all of the shares that Lincoln Park may be required to purchase on or after the date of this prospectus pursuant to the Purchase Agreement, because the issuance of such shares is solely at our discretion and is subject to certain conditions, the satisfaction of all of which are outside of Lincoln Park's control, including the registration statement of which this prospectus is a part becoming and remaining effective. Furthermore, under the terms of the Purchase Agreement, issuances and sales of shares of our common stock to Lincoln Park are subject to certain limitations on the amounts we may sell to Lincoln Park at any time, including the Exchange Cap and the Beneficial Ownership Cap. See the description under the heading "The Lincoln Park Transaction" for more information about the Purchase Agreement.
- (2) Immediately prior to the date of this prospectus, Lincoln Park beneficially owns 0 shares.
- (3) Assumes the sale to Lincoln Park pursuant to the Purchase Agreement of all shares of common stock registered pursuant to the registration statement that includes this prospectus. The selling stockholder is under no obligation known to us to resell any shares of common stock at this time.
- (4) Assumes the issuance of the maximum 4,500,000 shares that are offered for resale by Lincoln Park under this prospectus. The Purchase Agreement provides that we may sell up to \$25.0 million of our common stock to Lincoln Park. As of February 11, 2021, we have sold an aggregate of 1,338,299 shares of our common stock to Lincoln Park under the Purchase Agreement for an aggregate of approximately \$3.6 million, all of which shares (together with the 180,701 Commitment Shares) were registered for resale under the Prior Registration Statement. Depending on the market prices of our common stock at the time we elect to issue and sell such additional shares to Lincoln Park under the Purchase Agreement, we may need to sell more shares to Lincoln Park than are offered under this prospectus to receive aggregate gross proceeds equal to the \$21.4 million balance of the \$25.0 million total commitment available to us under the Purchase Agreement.

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Agreement, in which case we must first register for resale under the Securities Act additional shares of our common stock. Assuming a purchase price of \$3.08 (which represents the closing price of our common stock on February 24, 2021), the purchase by Lincoln Park of the entire 4,500,000 additional shares being registered for resale hereunder would result in gross proceeds to us of only approximately \$13.9 million, which together with the \$3.6 million we sold to Lincoln Park under the Purchase Agreement between the Commencement Date and February 11, 2021, would result in total gross proceeds to us of \$17.5 million of the \$25.0 million total commitment under the Purchase Agreement. The number of shares ultimately offered for resale by Lincoln Park will depend upon the number of shares we elect to sell to Lincoln Park under the Purchase Agreement.

- (5) Following the resale of all registered shares, Lincoln Park will beneficially own 0 shares.
- (6) Josh Scheinfeld and Jonathan Cope, the Managing Members of Lincoln Park Capital, LLC, the manager of the selling stockholder, are deemed to be beneficial owners of all of the shares of our common stock owned by the selling stockholder. Messrs. Cope and Scheinfeld have shared voting and investment power over the shares of our common stock being offered under this prospectus. Lincoln Park Capital, LLC is not a licensed broker-dealer or an affiliate of a licensed broker-dealer.

MARKET PRICE OF OUR COMMON STOCK AND RELATED STOCKHOLDER MATTERS

Market Information

Our common stock is traded on the Nasdaq Capital Market under the symbol “PSTV.”

Holders

As of February 24, 2021, there were approximately 14 registered holders of our common stock. This number does not include stockholders for whom shares were held in “nominee” or “street name.”

Dividend Policy

We have never declared or paid any cash dividends on our common stock and we do not intend to pay cash dividends in the foreseeable future. We currently expect to retain any future earnings to fund the operation and expansion of our business.

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, and some of the provisions of our certificate of incorporation and bylaws and of the Delaware General Corporation Law, or DGCL. 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 February 24, 2021, there were 9,166,902 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, and the shares of common stock offered, when issued, will be fully paid and nonassessable.

Preferred Stock

We are authorized to issue 5,000,000 shares of preferred stock, 1,954 shares of which were issued and outstanding as of December 31, 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

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- 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

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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.

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 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

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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 each class of preferred stock is Broadridge Corporate Issuer Solutions, Inc. The transfer agent's address is 1717 Arch Street, Suite 1300, Philadelphia, Pennsylvania 19103.

Listing

Our common stock is listed on the Nasdaq Capital Market under the symbol "PSTV."

PLAN OF DISTRIBUTION

The shares of our common stock offered by this prospectus are being offered by the selling stockholder, Lincoln Park. The shares may be sold or distributed from time to time by the selling stockholder directly to one or more purchasers or through brokers, dealers, or underwriters who may act solely as agents at market prices prevailing at the time of sale, at prices related to the prevailing market prices, at negotiated prices, or at fixed prices, which may be changed. The sale of the common stock offered by this prospectus could be effected in one or more of the following methods:

- ordinary brokers' transactions;
- transactions involving cross or block trades;
- through brokers, dealers, or underwriters who may act solely as agents;
- "at the market" into an existing market for our common stock;
- in other ways not involving market makers or established business markets, including direct sales to purchasers or sales effected through agents;
- in privately negotiated transactions; or
- any combination of the foregoing.

In order to comply with the securities laws of certain states, if applicable, the shares of our common stock offered by this prospectus may be sold only through registered or licensed brokers or dealers. In addition, in certain states, the shares of our common stock offered by this prospectus may not be sold unless they have been registered or qualified for sale in the state or an exemption from the state's registration or qualification requirement is available and complied with.

Lincoln Park is an "underwriter" within the meaning of Section 2(a)(11) of the Securities Act.

Lincoln Park has informed us that it intends to use an unaffiliated broker-dealer to effectuate all sales, if any, of our common stock that it may purchase from us pursuant to the Purchase Agreement. Such sales will be made at prices and at terms then prevailing or at prices related to the then current market price. Each such unaffiliated broker-dealer will be an underwriter within the meaning of Section 2(a)(11) of the Securities Act. Lincoln Park has informed us that each such broker-dealer will receive commissions from Lincoln Park that will not exceed customary brokerage commissions.

Brokers, dealers, underwriters or agents participating in the distribution of the shares of our common stock offered by this prospectus may receive compensation in the form of commissions, discounts, or concessions from the selling stockholder and/or the purchasers, for whom the broker-dealers may act as agent. The compensation paid to any such particular broker-dealer may be less than or in excess of customary commissions. Neither we nor Lincoln Park can presently estimate the amount of compensation that any agent will receive from the selling stockholder or from any purchasers of shares of our common stock sold by Lincoln Park.

We know of no existing arrangements between Lincoln Park or any other stockholder, broker, dealer, underwriter or agent relating to the sale or distribution of the shares of our common stock offered by this prospectus.

We may from time to time file with the SEC one or more supplements to this prospectus or amendments to the registration statement of which this prospectus forms a part to amend, supplement or update information contained in this prospectus, including, if and when required under the Securities Act, to disclose certain information relating to a particular sale of shares of our common stock offered by this prospectus by the selling stockholder, including the names of any brokers, dealers, underwriters or agents participating in the distribution of such shares of our common stock by the selling stockholder, any compensation paid by Lincoln Park to any such brokers, dealers, underwriters or agents, and any other required information.

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We will pay the expenses incident to the registration, offering and sale of the shares of our common stock to Lincoln Park. We have agreed to indemnify Lincoln Park and certain other persons against certain liabilities in connection with the offering of shares of common stock offered by this prospectus, including liabilities arising under the Securities Act or, if such indemnity is unavailable, to contribute amounts required to be paid in respect of such liabilities. Lincoln Park has agreed to indemnify us against liabilities under the Securities Act that may arise from certain written information furnished to us by Lincoln Park specifically for use in this prospectus or, if such indemnity is unavailable, to contribute amounts required to be paid in respect of such liabilities.

Lincoln Park has represented to us that at no time prior to the Purchase Agreement has Lincoln Park or its agents, representatives or affiliates engaged in or effected, in any manner whatsoever, directly or indirectly, any short sale (as such term is defined in Rule 200 of Regulation SHO of the Exchange Act) of our common stock or any hedging transaction, which establishes a net short position with respect to our common stock. Lincoln Park has agreed that during the term of the Purchase Agreement, it and its agents, representatives or affiliates will not enter into or effect, directly or indirectly, any of the foregoing transactions.

We have advised Lincoln Park that it is required to comply with Regulation M promulgated under the Exchange Act. With certain exceptions, Regulation M precludes the selling stockholder, any affiliated purchasers, and any broker-dealer or other person who participates in the distribution from bidding for or purchasing, or attempting to induce any person to bid for or purchase any security which is the subject of the distribution until the entire distribution is complete. Regulation M also prohibits any bids or purchases made in order to stabilize the price of a security in connection with the distribution of that security. All of the foregoing may affect the marketability of the securities offered by this prospectus.

This offering will terminate on the earlier of (i) termination of the Purchase Agreement or (ii) the date that all shares of our common stock offered by this prospectus have been sold by Lincoln Park.

Our common stock is listed on the Nasdaq Capital Market under the symbol "PSTV".

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, 2020 and 2019 and for the years then ended incorporated by reference in this prospectus 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-1 with the SEC under the Securities Act. 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 also 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 website address is www.sec.gov. The information on the SEC's website is not part of this prospectus, and any references to this website or any other website are inactive textual references only.

INCORPORATION BY REFERENCE

The SEC permits us to "incorporate by reference" the information contained in documents we have filed 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. 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, 2020 (filed with the SEC on February 22, 2021 and February 26, 2021, respectively);
- our Current Reports on Form 8-K filed with the SEC on [January 12, 2021](#) and [February 23, 2021](#) (each to the extent filed and not furnished);
- the description of our common stock contained in our Registration Statement on [Form 10/A](#) (File No. 000-32501) filed on July 16, 2001, and any amendment or report filed with the Commission for the purpose of updating the description.

We are not, however, incorporating, in each case, any documents or information that we are deemed to furnish and not file in accordance with SEC rules.

Any statement contained in any document incorporated by reference herein will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or any prospectus supplement modifies or supersedes such statement. Any statement so modified or superseded will not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering, including all such documents we may file with the SEC

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after the date of the initial registration statement and prior to the effectiveness of the registration statement, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus and deemed to be part of this prospectus from the date of the filing of such reports and documents.

We will provide without charge to each person, including any beneficial owner, to whom this prospectus is delivered, upon written or oral request, a copy of any or all documents that are incorporated by reference into this prospectus, but not delivered with the prospectus, other than exhibits to such documents unless such exhibits are specifically incorporated by reference into the documents that this prospectus incorporates. You should direct oral or written requests by one of the following methods. Attention: Investor Relations, Plus Therapeutics, Inc., 4200 Marathon Blvd., Suite 200, Austin, TX 78756, (737) 255-7194. You may also access these documents, free of charge on the SEC's website at www.sec.gov or on the "Investors" page of our 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.

DISCLOSURE OF COMMISSION POSITION ON INDEMNIFICATION FOR SECURITIES ACT LIABILITIES

Inssofar as indemnification for liabilities arising under the Securities Act may be permitted to our directors, officers, and controlling persons, we have been informed that in the opinion of the SEC this indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

4,500,000 Shares of Common Stock



PROSPECTUS

, 2021

PART II**Information Not Required in Prospectus****Item 13. Other Expenses of Issuance and Distribution.**

The following is a statement of estimated expenses in connection with the offering described in this registration statement. All expenses incurred with respect to the registration of the common stock will be borne by us. All amounts are estimates except the SEC registration fee.

	<u>Amount</u>
SEC Registration Fee	\$ 1,552
Printing Expenses	15,000
Legal Fees and Expenses	50,000
Accounting Fees and Expenses	25,000
Miscellaneous Expenses	8,448
Total	<u>\$ 100,000</u>

Item 14. Indemnification of Directors and Officers.

Section 102 of the Delaware General Corporation Law (the “DGCL”) allows a corporation to eliminate the personal liability of directors of a corporation to the corporation or its stockholders for monetary damages for breach of fiduciary duty as a director, except where the director breached the duty of loyalty, failed to act in good faith, engaged in intentional misconduct or knowingly violated a law, authorized the payment of a dividend or approved a stock repurchase in violation of the DGCL or obtained an improper personal benefit.

Section 145 of the DGCL provides, among other things, that we may indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding—other than an action by or in our right—by reason of the fact that the person is or was our director, officer, agent or employee, or is or was serving at our request as a director, officer, agent or employee of another corporation, partnership, joint venture, trust or other enterprise against expenses, including attorneys’ fees, judgments, fines and amounts paid in settlement actually and reasonably incurred by the person in connection with such action, suit or proceeding. The power to indemnify applies (a) if such person is successful on the merits or otherwise in defense of any action, suit or proceeding, or (b) if such person acting in good faith and in a manner he or she reasonably believed to be in the best interest, or not opposed to the best interest, of us, and with respect to any criminal action or proceeding had no reasonable cause to believe his or her conduct was unlawful. The power to indemnify applies to actions brought by or in our right as well but only to the extent of defense expenses, including attorneys’ fees but excluding amounts paid in settlement, actually and reasonably incurred and not to any satisfaction of judgment or settlement of the claim itself, and with the further limitation that in such actions no indemnification shall be made in the event of any adjudication of liability to us, unless the court believes that in light of all the circumstances indemnification should apply.

Section 174 of the DGCL provides, among other things, that a director who willfully or negligently approves of an unlawful payment of dividends or an unlawful stock repurchase or redemption may be held liable for such actions. A director who was either absent when the unlawful actions were approved or dissented at the time, may avoid liability by causing his or her dissent to such actions to be entered in the books containing minutes of the meetings of the board of directors at the time such action occurred or immediately after such absent director receives notice of the unlawful acts.

Our amended and restated certificate of incorporation, as amended, and amended and restated bylaws, filed as Exhibit 3.1 to our Annual Report on Form 10-K filed March 11, 2016 and Exhibit 3.2 to our Quarterly Report on Form 10-Q filed July 29, 2019, respectively, provide that we shall indemnify our directors, officers, employees and other agents to the fullest extent not prohibited by the DGCL or any other applicable law. In

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addition, we have entered into agreements to indemnify our directors and officers and expect to continue to enter into agreements to indemnify all of our directors and officers. These agreements require us, among other things, to indemnify our directors and officers against certain liabilities which may arise by reason of their status or service as directors or officers to the fullest extent not prohibited by law. These indemnification provisions and the indemnification agreements may be sufficiently broad to permit indemnification of our officers and directors for liabilities, including reimbursement of expenses incurred, arising under the Securities Act of 1933.

We maintain insurance policies under which our directors and executive officers are insured, within the limits and subject to the limitations of those policies, against certain expenses in connection with the defense of, and certain liabilities that might be imposed as a result of, actions, suits or proceedings to which they are parties by reason of being or having been directors or officers. The coverage provided by these policies may apply whether or not we would have the power to indemnify such person against such liability under the provisions of the General Corporation Law of the State of Delaware.

Item 15. Recent Sales of Unregistered Securities.

On September 30, 2020, we completed a private placement to Lincoln Park Capital Fund, LLC pursuant to which we have the right to sell to Lincoln Park up to \$25.0 million in shares of common stock, subject to certain limitations, from time to time over a 36-month period. We issued 180,701 Commitment Shares to Lincoln Park as consideration for its commitment to purchase our shares under the Purchase Agreement. In the Purchase Agreement, Lincoln Park represented to the Company, among other things, that it was an “accredited investor” (as such term is defined in Rule 501(a) of Regulation D under the Securities Act of 1933, or the Securities Act). The securities were sold by the Company under the Purchase Agreement in reliance upon an exemption from the registration requirements under the Securities Act afforded by Section 4(a)(2) of the Securities Act.

Item 16. Exhibits and Financial Statement Schedules.

(a) Exhibits.

The exhibits to the registration statement are listed in the Exhibit Index to this registration statement and are incorporated herein by reference.

(b) Financial Statement Schedules.

Financial statement schedules

All schedules have been omitted because either they are not required, are not applicable or the information is otherwise set forth in the financial statements and related notes thereto.

Item 17. Undertakings.

The undersigned registrant hereby undertakes:

- (1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:
 - (i) To include any prospectus required by section 10(a)(3) of the Securities Act of 1933;
 - (ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in

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the form of prospectus filed with the Securities and Exchange Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and

- (iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, however, that paragraphs (a)(1)(i), (a)(1)(ii) and (a)(1)(iii) above do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Securities and Exchange Commission by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

- (2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

- (3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

- (4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:

(A) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(B) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5) or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof. *Provided, however*, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

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

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

EXHIBIT INDEX

Exhibit No.	Exhibit Title	Filed herewith	Incorporated by Reference		
			Form	File No.	Date Filed
3.1	Composite Certificate of Incorporate		10-K	001-34375 Exhibit 3.1	03/11/2016
3.2	Certificate of Amendment to Amended and Restated Certificate of Incorporation.		8-K	001-34375 Exhibit 3.1	05/10/2016
3.3	Certificate of Amendment to Amended and Restated Certificate of Incorporation		8-K	001-34375 Exhibit 3.1	05/23/2018
3.4	Certificate of Amendment to Amended and Restated Certificate of Incorporation.		8-K	001-34375 Exhibit 3.1	07/29/2019
3.5	Certificate of Amendment to Amended and Restated Certificate of Incorporation.		8-K	001-34375 Exhibit 3.1	08/06/2019
3.6	Certificate of Designation of Preferences, Rights and Limitations of Series A 3.6% Convertible Preferred Stock		8-K	001-34375 Exhibit 3.1	10/08/2014
3.7	Certificate of Designation of Preferences, Rights and Limitations of Series B Convertible Preferred Stock		8-K	001-34375 Exhibit 3.1	11/28/2017
3.8	Certificate of Designation of Preferences, Rights and Limitations of Series C Convertible Preferred Stock		8-K	001-34375 Exhibit 3.1	07/25/2018
3.9	Amended and Restated Bylaws of Plus Therapeutics, Inc.		8-K	001-34375 Exhibit 3.2	07/29/2019
4.1	Description of Securities		10-K	001-34375 Exhibit 4.1	03/30/2020
4.2	Form of Common Stock Certificate		10-K	001-34375 Exhibit 4.33	03/09/2018
4.3	Form of Series T Warrant		POS AM	333-224502 Exhibit 4.28	07/09/2018
4.4	Form of Series T Warrant Agreement between Plus Therapeutics, Inc. and Broadridge Corporation Issuer Solutions, Inc. T Warrant Agreement between Plus Therapeutics, Inc.		POS AM	333-224502 Exhibit 4.36	07/09/2018
4.5	Form of Series U Warrant		S-1/A	333-229485 Exhibit 4.37	09/16/2019
4.6	Form of Warrant Amendment Agreement		8-K	011-34375 Exhibit 4.1	04/23/2020
4.7	Form of Underwriters' Warrant Amendment Agreement		8-K	011-34375 Exhibit 4.1	10/05/2020
5.1	Opinion of Pillsbury Winthrop Shaw Pittman LLP	X			

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Exhibit No.	Exhibit Title	Filed herewith	Incorporated by Reference		
			Form	File No.	Date Filed
10.1+	Patent and Know-How License Agreement, dated March 29, 2020, by and between Plus Therapeutics, Inc. and NanoTx, Corp.		8-K	011-34375 Exhibit 10.1	3/30/2020
10.2	Registration Rights Agreement between Plus Therapeutics, Inc. and Lincoln Park Capital Fund, LLC, dated September 30, 2020		8-K	001-34375 Exhibit 10.2	10/06/2020
10.3+	Asset Purchase Agreement by and between Plus Therapeutics, Inc. and Azaya Therapeutics, Inc., effective January 16, 2017		10-K	001-34375 Exhibit 10.40	03/24/2017
10.4	Loan and Security Agreement, dated May 29, 2015, by and between Plus Therapeutics, Inc. and Oxford Finance, LLC		10-Q	001-34375 Exhibit 10.4	08/10/2015
10.5	First Amendment to Loan and Security Agreement, dated September 20, 2017, by and between Plus Therapeutics, Inc. and Oxford Finance, LLC		S-1/A	333-219967 Exhibit 10.45	10/03/2017
10.6	Second Amendment to Loan and Security Agreement, dated June 19, 2018, by and between Plus Therapeutics, Inc. and Oxford Finance, LLC		10-Q	001-34375 Exhibit 10.3	08/14/2018
10.7	Third Amendment to Loan and Security Agreement, dated August 31, 2018, by and between Plus Therapeutics, Inc. and Oxford Finance, LLC		S-1	333-227485 Exhibit 10.51	09/21/2018
10.8	Fourth Amendment to Loan and Security Agreement dated December 31, 2018, by and between Plus Therapeutics, Inc. and Oxford Finance, LLC		S-1	333-229485 Exhibit 10.52	02/01/2019
10.9	Fifth Amendment to Loan and Security Agreement dated February 13, 2019, by and between Plus Therapeutics, Inc. and Oxford Finance, LLC		10-K	001-34375 Exhibit 10.55	03/29/2019
10.10	Sixth Amendment to Loan and Security Agreement dated March 4, 2019, by and between Plus Therapeutics, Inc. and Oxford Finance, LLC		10-K	001-34375 Exhibit 10.56	03/29/2019
10.11	Seventh Amendment to Loan and Security Agreement dated April 24, 2019, by and between Plus Therapeutics, Inc. and Oxford Finance, LLC		10-Q	001-34375 Exhibit 10.3	05/14/2019
10.12	Eight Amendment to Loan and Security Agreement dated July 15, 2019, by and between Plus Therapeutics, Inc. and Oxford Finance, LLC		10-Q	001-34375 Exhibit 10.2	08/15/2019
10.13+	Ninth Amendment to Loan and Security Agreement, dated March 29, 2020 by and between Plus Therapeutics, Inc. and Oxford Finance, LLC		8-K	011-34375 Exhibit 10.2	3/30/2020

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Exhibit No.	Exhibit Title	Filed herewith	Incorporated by Reference		
			Form	File No.	Date Filed
10.14#	Amended and Restated Employment Agreement between Marc Hedrick and Plus Therapeutics, Inc.		10-Q	001-34375 Exhibit 10.6	5/16/2020
10.15#	Amended and Restated Employment Agreement between Andrew Sims and Plus Therapeutics, Inc.		10-Q	001-34375 Exhibit 10.7	5/16/2020
10.16#	2014 Equity Incentive Plan of Plus Therapeutics, Inc., as amended and restated		10-Q	001-34375 Exhibit 10.3	08/15/2019
10.17#	2015 New Employee Incentive Plan		8-K	001-34375 Exhibit 10.1	01/05/2016
10.18#	First Amendment to the Plus Therapeutics, Inc. 2015 New Employee Incentive Plan, dated Jan. 26, 2017		10-K	001-34375 Exhibit 10.42	03/24/2017
10.19#	Second Amendment to the Plus Therapeutics, Inc. 2015 New Employee Incentive Plan, dated February 6, 2020		10-K	001-34375 Exhibit 10.25	03/30/2020
10.20#	Form of Notice of Grant of Stock Option under the 2015 New Employee Incentive Plan		S-8	333-210211 Exhibit 99.5	03/15/2016
10.21#	Form of Stock Option Agreement under the 2015 New Employee Incentive Plan		S-8	333-210211 Exhibit 99.4	03/15/2016
10.22#	2020 Stock Incentive Plan		S-8	001-34375 Exhibit 99.1	06/30/2020
10.23#	Purchase Agreement between Lincoln Park Capital Fund, LLC and Plus Therapeutics, Inc.		8-K	001-34375 Exhibit 10.1	10/06/2020
10.24+	Master Services Agreement between Piramal Pharma Solutions, Inc. and Plus Therapeutics, Inc.		10-K	001-334275 Exhibit 10.24	02/22/2021
10.25#	Form Indemnification Agreement		8-K	001-34375 Exhibit 10.1	02/06/2020
10.26#	Form of Agreement for Acceleration and/or Severance		10-K	001-34375 Exhibit 10.113	03/11/2016
23.1	Consent of BDO USA, LLP, Independent Registered Public Accounting Firm	X			
23.2	Consent of Pillsbury Winthrop Shaw Pittman LLP (included in Exhibit 5.1)	X			
24.1	Power of Attorney (see signature page)	X			

Indicates management contract or compensatory plan or arrangement.

+ Portions of this exhibit have been excluded pursuant to Item 601(b)(1)(iv).

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the Registrant has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Austin, State of Texas, on February 26, 2021.

PLUS THERAPEUTICS, INC.

By: /s/ Marc H. Hedrick, MD
President and Chief Executive Officer.

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints Marc H. Hedrick, MD and Andrew Sims, and each of them, his or her true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments, including post-effective amendments, to this Registration Statement, and any registration statement relating to the offering covered by this Registration Statement and filed pursuant to Rule 462(b) under the Securities Act of 1933, and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done, as fully for all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that each of said attorneys in fact and agents or their substitute or substitutes may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

<u>Name</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Marc H. Hedrick, MD</u> Marc H. Hedrick, MD	President and Chief Executive Officer and Director <i>(Principal Executive Officer)</i>	February 26, 2021
<u>/s/ Andrew Sims</u> Andrew Sims	Chief Financial Officer <i>(Principal Financial Officer and Principal Accounting Officer)</i>	February 26, 2021
<u>/s/ Richard J. Hawkins</u> Richard J. Hawkins	Chairman of the Board	February 26, 2021
<u>/s/ Howard Clowes</u> Howard Clowes	Director	February 26, 2021
<u>/s/ An van Es-Johansson, MD</u> An van Es-Johansson, MD	Director	February 26, 2021
<u>/s/ Robert Lenk, Ph.D.</u> Robert Lenk, Ph.D.	Director	February 26, 2021
<u>/s/ Greg Petersen</u> Greg Petersen	Director	February 26, 2021

PILLSBURY WINTHROP SHAW PITTMAN LLP
2550 Hanover Street
Palo Alto, California 94304

February 26, 2021

Plus Therapeutics, Inc.
4200 Marathon Blvd., Suite 200
Austin, TX 78756

Re: Registration Statement on Form S-1

Ladies and Gentlemen:

We are acting as counsel for Plus Therapeutics, Inc., a Delaware corporation (the "Company"), in connection with the Registration Statement on Form S-1 (the "Registration Statement") filed by the Company with the Securities and Exchange Commission (the "Commission") for purposes of registering under the Securities Act of 1933 (the "Act") the resale of 4,500,000 shares (the "Shares") of the Company's common stock, par value \$0.001 per share, which Shares are reserved for issuance pursuant to a purchase agreement between the Company and Lincoln Park Capital Fund, LLC, dated as of September 30, 2020 (the "Purchase Agreement").

We have reviewed and are familiar with such corporate proceedings and other matters as we have considered relevant or necessary for the opinions expressed in this letter. Based on the foregoing and the assumption that no Purchase Shares will be sold at a price which is less than the Floor Price (as defined in the Purchase Agreement), we are of the opinion that the Shares have been duly authorized and, when issued and delivered by the Company in the manner described in the Registration Statement and the Prospectus and in accordance with the resolutions adopted by the Board of Directors of the Company, will be validly issued, fully paid and non-assessable.

We hereby consent to the filing of this opinion letter as Exhibit 5.1 to the Registration Statement and to the use of our name under the caption "Legal Matters" in the Registration Statement and in the Prospectus included therein. In giving this consent, we do not thereby admit that we are within the category of persons whose consent is required under Section 7 of the Act or the rules and regulations of the Commission promulgated thereunder.

Very truly yours,

/s/ Pillsbury Winthrop Shaw Pittman LLP

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

Plus Therapeutics, Inc.
Austin, Texas

We hereby consent to the incorporation by reference in the Prospectus constituting a part of this Registration Statement of our report dated February 22, 2021, relating to the consolidated financial statements of Plus Therapeutics, Inc. (the “Company”) appearing in the Company’s Annual Report on Form 10-K for the year ended December 31, 2020. Our report contains an explanatory paragraph regarding the Company’s ability to continue as a going concern.

We also consent to the reference to us under the caption “Experts” in the Prospectus.

/s/ BDO USA, LLP

San Diego, California

February 26, 2021