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

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**AMENDMENT NO. 1  
TO  
Form S-1  
REGISTRATION STATEMENT**  
*Under  
The Securities Act of 1933*

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**PLUS THERAPEUTICS, INC.**

(Exact name of Registrant as specified in its charter)

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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)

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Andrew Sims  
Chief Financial 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)

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*Copies to:*

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Houston, TX 77002  
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**Approximate date of commencement of proposed sale to the public:** As soon as practicable after this registration statement is declared effective.

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   
Non-accelerated filer

Accelerated filer   
Smaller reporting company   
Emerging growth company

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

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**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.

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**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 March 8, 2024)**



Up to \_\_\_\_\_ Shares of Common Stock

Pre-Funded Warrants to purchase up to _____	Shares of Common Stock
Common Warrants to purchase up to _____	Shares of Common Stock
Shares of Common Stock underlying Pre-Funded Warrants and Common Warrants	
Placement Agent Warrants to Purchase up to _____	Shares of Common Stock
Shares of Common Stock Underlying the Placement Agent Warrants	

We are offering up to \_\_\_\_\_ shares of our common stock, together with warrants to purchase up to \_\_\_\_\_ shares of common stock, each a common warrant, at an assumed combined public offering price of \$ \_\_\_\_\_, which is equal to the closing price per share of our common stock on The Nasdaq Capital Market, on \_\_\_\_\_, 2024 (and the shares issuable from time to time upon exercise of the common warrants), pursuant to this prospectus. The shares of common stock and common warrants will be separately issued but must be purchased together in this offering. Each share of common stock is being offered together with a common warrant to purchase one share of common stock. Each common warrant will have an exercise price of \$ \_\_\_\_\_ per share, will be exercisable upon issuance, and will expire five (5) years from the date of issuance.

We are also offering to each purchaser whose purchase of shares of our common stock in this offering would otherwise result in the purchaser, together with its affiliates and certain related parties, beneficially owning more than 4.99% (or, at the election of the holder, 9.99%) of our outstanding shares of common stock immediately following the consummation of this offering, the opportunity to purchase, if the purchaser so chooses, pre-funded warrants to purchase shares of common stock, or the pre-funded warrants, in lieu of shares of common stock. Each pre-funded warrant will be exercisable for one share of our common stock. Pre-funded warrants will be exercisable upon issuance and will expire when exercised in full. The pre-funded warrants and accompanying common warrants will be separately issued, but must be purchased together in this offering. The purchase price of each pre-funded warrant will equal the price per share of common stock being sold to the public in this offering, minus \$0.001, and the exercise price of each pre-funded warrant will be \$0.001 per share. For each pre-funded warrant that we sell, the number of shares of our common stock that we are offering will be decreased on a one-for-one basis. The pre-funded warrants will not be listed on the Nasdaq Capital Market and are not expected to trade in any market, however we anticipate that the shares of our common stock to be issued upon exercise of the pre-funded warrants will trade on the Nasdaq Capital Market. This prospectus also relates to the shares of common stock issuable upon the exercise of the pre-funded warrants, common warrants, and placement agent warrants.

This offering will terminate on \_\_\_\_\_, unless we decide to terminate the offering (which we may do at any time in our discretion) prior to that date. We will have one closing for all the securities purchased in this offering. The combined public offering price per share (or pre-funded warrant) and common warrant will be fixed for the duration of this offering.

We have engaged \_\_\_\_\_, or the placement agent, to act as our exclusive placement agent in connection with this offering. The placement agent has agreed to use its reasonable best efforts to arrange for the sale of the securities offered by this prospectus. The placement agent is not purchasing or selling any of the securities we are offering and the placement agent is not required to arrange the purchase or sale of any specific number or dollar amount of securities. We have agreed to pay to the placement agent the placement agent fees set forth in the table below, which assumes that we sell all of the securities offered by this prospectus. Because we will deliver the securities to be issued in this offering upon our receipt of investor funds, there is no arrangement for funds to be received in escrow, trust or similar arrangement. There is no minimum offering requirement as a condition of closing of this offering. Because there is no minimum offering amount required as a condition to closing this offering, we may sell fewer than all of the securities offered hereby, which may significantly reduce the amount of proceeds received by us, and investors in this offering will not receive a refund in the event that we do not sell an amount of securities sufficient to pursue our business goals described in this prospectus. In addition, because there is no escrow account and no minimum offering amount, investors could be in a position where they have invested in our company, but we are unable to fulfill all of our contemplated objectives due to a lack of interest in this offering. Further, any proceeds from the sale of securities offered by us will be available for our immediate use, despite uncertainty about whether we would be able to use such funds to effectively implement our business plan. See the section entitled "Risk Factors" for more information. We will bear all costs associated with the offering. See "Plan of Distribution" on page 29 of this prospectus for more information regarding these arrangements.

Our common stock is listed on the Nasdaq Capital Market under the symbol "PSTV." The closing price of our common stock on the Nasdaq Stock Market on \_\_\_\_\_, 2024, was \$ \_\_\_\_\_ per share.

All share, common warrant, and pre-funded warrant numbers are based on an assumed combined public offering price of \$ \_\_\_\_\_ per share and the accompanying common warrant and \$ \_\_\_\_\_ per pre-funded warrant and the accompanying common warrant. The actual combined public offering price per share and common warrant and the actual combined public offering price per pre-funded warrant and common warrant will be determined through negotiation among us, the placement agent and the investors in the offering based on market conditions at the time of pricing, and may be at a discount to the current market price of our common stock. Therefore, the recent market price per share of common stock used throughout this prospectus as an assumed combined public offering price may not be indicative of the final offering price. There is no established trading market for the pre-funded warrants or the common warrants, and we do not expect a market to develop. We do not intend to apply for a listing of the pre-funded warrants or the common warrants on any securities exchange or other nationally recognized trading system. Without an active trading market, the liquidity of the pre-funded warrants and the common warrants will be limited.

Investing in our securities involves a high degree of risk. These risks are described in the "Risk Factors" section on page 11 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.

	Per Share and Accompanying Common Warrant	Per Pre-Funded Warrant and Accompanying Common Warrant	Total
Public offering price	\$ _____	\$ _____	\$ _____
Placement agent's fees <sup>(1)</sup>	\$ _____	\$ _____	\$ _____
Proceeds to us, before expenses <sup>(2)</sup>	\$ _____	\$ _____	\$ _____

(1) In addition, we have also agreed to pay the placement agent a management fee of 1.0% of the aggregate gross proceeds raised in this offering and to pay the placement agent for certain of its offering-related expenses. In addition, we have agreed to issue the placement agent or its designees, as compensation in connection with this offering, warrants, or the placement agent warrants, to purchase a number of shares of common stock equal to 7.0% of the shares of common stock sold in this offering (including the shares of common stock issuable upon the exercise of the pre-funded warrants), at an exercise price of \$ \_\_\_\_\_ per share, which represents 125% of the combined public offering price per share of common stock and accompanying common warrant. See "Plan of Distribution" for a description of the compensation to be received by the placement agent.

(2) Because there is no minimum number of securities or amount of proceeds required as a condition to closing in this offering, the actual public offering amount, placement agent fees, and proceeds to us, if any, are not presently determinable and may be substantially less than the total maximum offering amounts set forth above. For more information, see "Plan of Distribution."

Delivery of the securities offered hereby is expected to be made on or about \_\_\_\_\_, subject to satisfaction of customary closing conditions.

**The date of this prospectus is \_\_\_\_\_, 2024**

TABLE OF CONTENTS

<a href="#">ABOUT THIS PROSPECTUS</a>	ii
<a href="#">PROSPECTUS SUMMARY</a>	1
<a href="#">THE OFFERING</a>	8
<a href="#">RISK FACTORS</a>	11
<a href="#">FORWARD-LOOKING STATEMENTS</a>	14
<a href="#">USE OF PROCEEDS</a>	15
<a href="#">DILUTION</a>	16
<a href="#">DESCRIPTION OF CAPITAL STOCK</a>	19
<a href="#">DESCRIPTION OF SECURITIES WE ARE OFFERING</a>	25
<a href="#">PLAN OF DISTRIBUTION</a>	29
<a href="#">LEGAL MATTERS</a>	33
<a href="#">EXPERTS</a>	33
<a href="#">WHERE YOU CAN FIND MORE INFORMATION</a>	33
<a href="#">INCORPORATION BY REFERENCE</a>	34

## ABOUT THIS PROSPECTUS

You should read this prospectus and the related exhibits filed with the Securities and Exchange Commission (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 placement agent, 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 placement agent, 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.

### Industry and Market Data

This prospectus and the documents incorporated by reference contain estimates, projections and other information concerning our industry, our business, the science of our products and the markets for our products, including data regarding the incidence of certain medical conditions and the scientific basis of our products. We obtained the industry, science, market and similar data set forth in this prospectus from our internal estimates and research and from academic and industry research, publications, surveys, and studies conducted by third parties. While we believe that these industry publications and third-party research, surveys and studies are reliable, we have not independently verified such data and we do not make any representation as to the accuracy of the information. The content of the above sources, except to the extent specifically set forth in this prospectus, does not constitute a portion of this prospectus and is not incorporated herein. Information that is based on estimates, forecasts, projections, market research, scientific research, or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are assumed in this information.

## 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**

#### **Overview**

We are a U.S. pharmaceutical company developing targeted radiotherapeutics with advanced platform technologies for central nervous system (“CNS”) cancers. Our novel radioactive drug formulations and therapeutic candidates are designed to deliver safe and effective doses of radiation to tumors. To achieve this, we have developed innovative approaches to drug formulation, including encapsulating radionuclides such as rhenium isotopes with nanoliposomes and microspheres. Our formulations are intended to achieve elevated patient absorbed radiation doses and extend retention times such that the clearance of the isotope occurs after significant and essentially complete radiation decay, which will contribute and provide less normal tissue/organ exposure and improved safety margins.

Traditional approaches to radiation therapy for cancer such as external beam radiation have many disadvantages including continuous treatment for four to six weeks (which is onerous for patients), that the radiation damages healthy cells and tissue, and that the amount of radiation delivered is very limited and, therefore, is frequently inadequate to fully destroy the cancer.

Our targeted radiotherapeutic platform and investigational drugs have the potential to overcome these disadvantages by directing higher, more powerful radiation doses at the tumor—and only the tumor—potentially in a single treatment. By minimizing radiation exposure to healthy tissues while simultaneously maximizing locoregional delivery and, thereby, efficacy, we hope to reduce the radiation toxicity for patients, improving their quality of life and life expectancy. Our radiotherapeutic platform, combined with advances in surgery, nuclear medicine, interventional radiology, and radiation oncology, affords us the opportunity to target a broad variety of cancer types.

Our lead radiotherapeutic candidate, rhenium (<sup>186</sup>Re) obisbameda (formerly “<sup>186</sup>RNL”), is designed specifically for CNS cancers including recurrent glioblastoma (“GBM”), leptomeningeal metastases (“LM”), and pediatric brain cancers (“PBC”) by direct localized delivery utilizing approved standard-of-care tissue access such as with convection-enhanced delivery (“CED”) and intraventricular brain (Ommaya reservoir) catheters. Our acquired radiotherapeutic candidate, Rhenium-188 NanoLiposome Biodegradable Alginate Microsphere (“<sup>188</sup>RNL-BAM”) is designed to treat many solid organ cancers including primary and secondary liver cancers by intra-arterial injection.

Our headquarters and manufacturing facilities are in Texas and are in proximity to world-class cancer institutions and researchers. Our dedicated team of engineers, physicians, scientists, and other professionals are committed to advancing our targeted radiotherapeutic technology for the benefit of cancer patients and healthcare providers worldwide and our current pipeline is focused on treating rare and difficult-to-treat cancers with significant unmet medical needs.

In addition to our headquarters in Austin, we have an established, GMP-validated research and development and manufacturing facility in San Antonio, Texas, tailored to produce Current Good Manufacturing Practice (“cGMP”) rhenium (<sup>186</sup>Re) obisbameda. We have built a supply chain through strategic partnerships that

enable the development, manufacturing and future potential commercialization of our products. Our current supply chain and key partners are positioned to supply cGMP rhenium (186Re) obisbameda for ongoing and planned Phase 2 and Phase 3 clinical trials in patients with GBM, LM and PBC.

### *Pipeline*

Our most advanced investigational drug, rhenium (186Re) obisbameda, is a patented radiotherapy potentially useful for patients with CNS and other cancers. Preclinical study data describing the use of rhenium (186Re) obisbameda for several cancer targets have been published in peer-reviewed journals and reported at a variety of medical society peer-reviewed meetings. Besides, GBM, LM and PBC, rhenium (186Re) obisbameda has been reported to have potential applications for head and neck cancer, ovarian cancer, breast cancer and peritoneal metastases.

The rhenium (186Re) obisbameda technology was part of a licensed radiotherapeutic portfolio that we acquired from NanoTx, Corp. on May 7, 2020. The licensed radiotherapeutic has been evaluated in preclinical studies for several cancer targets and we have an active \$3.0 million award from U.S. National Institutes of Health/National Cancer Institute which is expected to provide financial support for the continued clinical development of rhenium (186Re) obisbameda for recurrent GBM through the completion of a Phase 2 clinical trial including enrollment of up to 55 patients.

On August 29, 2022, we announced feedback from a Type C meeting with the U.S. Food and Drug Administration (the “FDA”) regarding Chemistry, Manufacturing and Controls (“CMC”) practices. The meeting focused on our cGMP clinical and commercial manufacturing process for our lead investigational targeted radiotherapeutic, BMEDA-chelated rhenium (186Re) obisbameda, for recurrent GBM.

The FDA indicated agreement with our proposed application of cGMP guidance for radiotherapeutics, small molecule drug products and liposome drug products for our novel rhenium (186Re) obisbameda in support of ongoing and future GBM clinical trials, manufacturing scale up, and commercialization. Alignment with the FDA includes support of our proposed controls and release strategy for new drug substance and new drug product. Because this product is identical for recurrent GBM, LM, and PBC, we believe alignment will be consistent for rhenium (186Re) obisbameda used in other clinical development programs, including LM and PBC.

### *Rhenium (186Re) obisbameda versus External Beam Radiation Therapy for Recurrent GBM*

Rhenium (186Re) obisbameda is a novel injectable radiotherapy designed to deliver targeted, high dose radiation directly into GBM tumors in a safe, effective, and convenient manner that may ultimately prolong patient survival. Rhenium (186Re) obisbameda is composed of the radionuclide Rhenium-186 and a nanoliposomal carrier, and is infused in a highly targeted, controlled fashion, directly into the tumor via precision brain mapping and CED catheters. Potential benefits of rhenium (186Re) obisbameda compared to standard external beam radiotherapy include:

- The rhenium (186Re) obisbameda radiation dose delivered to patients may be up to 20 times greater than what is possible with commonly used external beam radiation therapy (“EBRT”), which, unlike EBRT and proton beam devices, spares normal tissue and the brain from radiation exposure.
- Rhenium (186Re) obisbameda can be visualized in real-time during administration, possibly giving clinicians better control of radiation dosing, distribution and retention.
- Rhenium (186Re) obisbameda potentially more effectively treats a bulk tumor and microscopic disease that has already invaded healthy tissue.
- Rhenium (186Re) obisbameda is infused directly into the targeted tumor by CED catheter insertion using MRI guided software to avoid critical patient neurological structures and neural pathways and

also bypasses the blood brain barrier, which delivers the therapeutic product where it is needed. Importantly, it reduces radiation exposure to healthy cells, in contrast to EBRT which passes through normal tissue to reach the tumor, continuing its path through the tumor, hence being less targeted and selective.

- Rhenium (<sup>186</sup>Re) obisbameda is given during a single, short, in-patient hospital visit, and is available in all hospitals with nuclear medicine and neurosurgery, while EBRT requires out-patient visits five days a week for approximately four to six weeks.

#### *ReSPECT-GBM Trial for Recurrent GBM*

Recurrent GBM is the most common, complex, and aggressive primary brain cancer in adults. In the U.S., there are more than 13,000 GBM cases diagnosed and approximately 10,000 patients succumb to the disease each year. The average length of overall survival (“OS”) for GBM patients is eight months, with a one-year survival rate of 40.8% and a five-year survival rate of only 6.8% and these estimates vary and are lower in some publications. GBM routinely presents with headaches, seizures, vision changes and other significant neurological complications, with a significant compromise in quality of life. Despite the best available medical treatments, the disease remains incurable. Even after efforts to manage the presenting signs and symptoms and completely resect the initial brain tumor, some microscopic disease almost always remains and tumor regrowth occurs within months. Approximately 90% or more of patients with primary GBM experience tumor recurrence. Complete surgical removal of GBM is usually not possible and GBM is often resistant or quickly develops resistance to most available current and investigational therapies. Even today, the treatment of GBM remains a significant challenge and it has been nearly a decade since the FDA approved a new therapy for this disease, and these more recent approvals have not improved GBM patients’ OS over past decades, and significant unmet medical need persists.

For recurrent GBM, there are few currently approved treatments, which in the aggregate, provide only marginal survival benefit. Furthermore, these therapies are associated with significant side effects, which limit dosing and prolonged use.

While EBRT has been shown to be safe and has temporary efficacy in many malignancies, including GBM, typically at absorbed, fractionated radiation dose of ~30 Gray in GBM, this maximum possible administered dose is always limited by toxicity to the normal tissues surrounding the malignancy, and because EBRT requires fractionation to manage toxicity and maximum EBRT limits are typically reached before long-term efficacy reached. Because of this limitation, EBRT cannot provide a cure or long term control of GBM and GBM always recurs within months after EBRT. In contrast, locally delivered and targeted radiopharmaceuticals that precisely deliver radiation in the form of beta particles such as Iodine-131 for thyroid cancer, are known to be safe and effective and minimize exposure to normal cells and tissues especially with optimal administered dose and minimizing exposure to normal tissue. The locally delivered rhenium (<sup>186</sup>Re) obisbameda is designed for and provides patient tolerability and safety. Though no rhenium (<sup>186</sup>Re) obisbameda head-to-head trial with chemo, immune, EBRT or systemic radiopharmaceutical products have been conducted, patient tolerability and safety considerations have been reported as expected.

Interim results from our ongoing Phase 1/2a ReSPECT-GBM trial (ClinicalTrials.gov NCT01906385) show that the beta particle energy from our lead investigational drug rhenium (<sup>186</sup>Re) obisbameda has provided preliminary positive data and utility in treating GBM and potential other malignancies. More specifically, the preliminary data from our Phase 1/2a ReSPECT-GBM trial suggests that radiation, in the form of high energy beta particles or electrons, can be effective against GBM. Thus far, we have been able to deliver up to 740 Gy of absorbed radiation to tumor tissue in humans, without significant or dose limiting toxicities and with what we believe has the capability to go higher if required. In comparison, current EBRT protocols for recurrent GBM typically recommend a total maximum radiation dose of about ~30-35 Gray.



In September 2020, the FDA granted both Orphan Drug and Fast Track designations to rhenium (186Re) obisbameda for the treatment of patients with GBM. In November 2021, the FDA granted Fast Track designation for rhenium (186Re) obisbameda for the treatment of LM.

Rhenium (186Re) obisbameda is under clinical investigation in a multicenter, sequential cohort, open-label, volume and dose escalation study of the safety, tolerability, and distribution of rhenium (186Re) obisbameda given by CED catheters to patients with recurrent or progressive malignant glioma after standard surgical, radiation, and/or chemotherapy treatment (NCT01906385). The study uses a standard, modified 3x3 Fibonacci dose escalation, followed by a planned Phase 2 expansion trial at the maximum tolerated dose (“MTD”)/maximum feasible dose (“MFD”) or non-dose limiting toxicity (“DLT”) if MTD is not reached, to determine efficacy. The trial is funded through Phase 2 in large part by a NIH/NCI grant. These investigations have not reached DLT or MTD/MFD and the study is in its eighth dosing administration cohort. Due to the observation of a preliminary efficacy signal, we have initiated in parallel a Phase 2, non-DLT dose trial pursuant to the currently funded NIH/NCI grant. This trial will begin at the current non-DLT rhenium (186Re) obisbameda dose and will expand exploring higher radiation doses in larger volumes to treat larger tumors. Additionally, two or more rhenium (186Re) obisbameda administrations, if indicated, will be evaluated, and reviewed with the FDA, as well as expanded safety, imaging and efficacy data to support a planned future registrational trial.

On September 6, 2022, we announced a summary of our Type C clinical meeting with the FDA that focused on the ReSPECT-GBM trial. The FDA agreed with us that the ReSPECT-GBM clinical trial should proceed to the planned Phase 2. The key focus areas of clinical investigation of the Phase 2 trial will be (1) further dose exploration, including both increased dosing and multiple doses, and (2) collecting additional safety and efficacy data to inform the design of a future registrational trial. Because no DLT administered doses were observed, the FDA and we also agreed to continue to dose cohort eight. There was further agreement with the FDA that in a planned future registrational trial, overall survival should be used as the primary endpoint. We agreed with the FDA to hold future meetings to consider the use of external data to augment the use of a control arm in the registrational trial.

On January 18, 2023, we announced that the first patient has been dosed in the ReSPECT-GBM Phase 2b dose expansion clinical trial evaluating rhenium obisbameda for the treatment of recurrent GBM. The Phase 2b trial is expected to enroll up to 31 total patients with small- to medium-sized tumors and is targeted for full enrollment by the end of 2024, with the plan to add additional clinical sites to support the trial and an initial data read-out by the end of 2024.

In June 2023, we presented data regarding the safety and feasibility results from our Phase 1/2 Clinical Trial of 186RNL (Rhenium-186 Nanoliposome) (186) Obisbameda in Recurrent Glioma: The ReSPECT-GBM Trial at the Society of Nuclear Medicine & Molecular Imaging Annual Meeting.

On November 20, 2023, we announced positive data from the ongoing ReSPECT-GBM Phase 2 trial evaluating our lead radiotherapeutic, rhenium (186Re) obisbameda, for the treatment of recurrent glioblastoma at the Society for NeuroOncology 28th Annual Meeting, which was held November 15-19, 2023 in Vancouver, Canada.

Key findings included:

- Median overall survival in 15 patients with recurrent glioblastoma (“rGBM”) from the Phase 2 study is 13 months, which is 63% better than current standard of care (bevacizumab monotherapy) of 8 months; 9 of the 15 patients remain alive.
- Median progression free survival is 11 months, compared to SOC at 4 months.

- Rhenium (186Re) obisbameda continues to demonstrate a favorable safety profile, despite delivering up to 20x the dose of radiation (up to 740 Gy) typically delivered by EBRT for rGBM patients (up to 35 Gy).
- Imaging data presented by Andrew Brenner, MD, PhD is consistent with the efficacy signal of Rhenium (186Re) obisbameda in rGBM.

On March 31, 2022, we entered into a Sales Order (the “Sales Order”) with Medidata Solutions, Inc. (“Medidata”), pursuant to which Medidata built a Synthetic Control Arm® platform that facilitates the use of historical clinical data to incorporate into our Phase 2 clinical trial of rhenium (186Re) obisbameda in GBM. The Sales Order had a term of six months. Work under this Sales Order has been completed. As part of this collaboration, we jointly submitted with Medidata a historical clinical trials control arm methodology abstract (“HCA”) to the American Society of Clinical Oncology which was accepted for publication, further strengthening this collaboration and allowing applications to advance GBM development. We plan to use the HCA for breakthrough therapy designation and Phase 2 and/or a pivotal or registrational Phase 3 trial.

#### *ReSPECT-LM Clinical Trial for LM*

LM is a rare complication of cancer in which the disease spreads to the membranes (meninges) surrounding the brain and spinal cord. The incidence of LM is growing and occurs in approximately 5% or more of people with late-stage cancer, or 110,000 people in the U.S. each year. It is highly lethal with an average one-year survival of just 7%. All solid cancers, particularly breast, lung, GI, and melanoma, have the potential to spread to the leptomeninges.

The ReSPECT-LM Phase 1 clinical trial (ClinicalTrials.gov NCT05034497) was preceded with preclinical studies in which tolerance to doses of rhenium (186Re) obisbameda as high as 1,075 Gy were shown in animal models with LM without significant observed toxicity. Furthermore, treatment led to a marked reduction in tumor burden in both C6 and MDA-231 LM models.

Upon receiving acceptance of our Investigational New Drug application and Fast Track designation by the FDA for rhenium (186Re) obisbameda for the treatment of LM, we initiated the trial and began screening patients for the ReSPECT-LM Phase 1 clinical trial in Q4 2021. The ReSPECT-LM is a multi-center, sequential cohort, open-label, dose escalation study evaluating the safety, tolerability, and efficacy of a single-dose application of rhenium (186Re) obisbameda administered through intrathecal infusion to the ventricle of patients with LM after standard surgical, radiation, and/or chemotherapy treatment. The primary endpoint of the study is the incidence and severity of adverse events and dose limiting toxicities, together with determining the maximum tolerated and recommended Phase 2 dose. Full enrollment in the Phase I trial is expected by the end of 2024, with the plan to add additional clinical sites to support the trial.

On September 19, 2022, we entered into a Cancer Research Grant Contract (the “CPRIT Contract”), effective as of August 31, 2022, with CPRIT, pursuant to which CPRIT will provide us a grant of up to \$17.6 million (the “CPRIT Grant”) over a three-year period to fund the continued development of rhenium (186Re) obisbameda for the treatment of patients with LM through Phase 2 of the ReSPECT LM clinical trial. The CPRIT Grant is subject to customary CPRIT funding conditions, including, but not limited to, a matching fund requirement (one dollar from us for every two dollars awarded by CPRIT), revenue sharing obligations upon commercialization of rhenium (186Re) obisbameda based on specific dollar thresholds until CPRIT receives the aggregate amount of 400% of the proceeds awarded under the CPRIT Grant, and certain reporting requirements.

Interim results showed that a single treatment with rhenium (186Re) obisbameda showed a consistent decreased cerebrospinal fluid (“CSF”) tumor cell count/ml and was very well tolerated by all LM patients.

Rhenium (<sup>186</sup>Re) obisbameda is an outpatient administration and treatment and is easily and safely administered through a standard intraventricular catheter (Ommaya Reservoir), distributed promptly throughout the CSF, and with durable retention in the leptomeninges at least through day seven. All patients have shown well tolerated prompt and durable rhenium (<sup>186</sup>Re) obisbameda distribution throughout the subarachnoid space. On October 10, 2023, we announced we had completed Cohort 4 of the ReSPECT-LM Phase 1/2a dose escalation trial.

A single dose of rhenium (<sup>186</sup>Re) obisbameda at 6.6 millicurie (“mCi”) in 5.0 mL, in Cohort 1, achieved absorbed doses of 18.7 to 29.0 Gy to the ventricles and cranial subarachnoid spaces, respectively. Cohort 2 has also completed with a 13.2 mCi administered dose in 5ml and was also well tolerated. Cohort 3 enrolled three patients through early April 2023 with a 26.4 mCi administered dose.

On August 10, 2023, we presented data from the ReSPECT-LM clinical trial of rhenium (<sup>186</sup>Re) obisbameda at American Society of Clinical Oncology CNS Cancer Conference.

In November 2023, the FDA granted Orphan Drug designation to rhenium (<sup>186</sup>Re) obisbameda for the treatment of patients with breast cancer with LM.

On December 12, 2023, we announced our partnership with K2bio to implement novel analysis for CSF tumor and molecular biomarkers for CNS cancers. Initial clinical specimen processing and testing will begin in the first quarter 2024 in our ongoing Phase 1 ReSPECT-LM trial of rhenium (<sup>186</sup>Re) obisbameda in patients with LM.

#### *ReSPECT-PBC Clinical Trial for Pediatric Brain Cancer*

The average annual age adjusted mortality rate for children aged 0-14 for malignant brain (and other CNS) tumors is 0.71/100,000, making it the most common cause of death and cancer death in this age group. The 2021 World Health Organization Classification of CNS Tumors classifies gliomas, glioneuronal tumors, and neuronal tumors into six different families: (1) adult-type diffuse gliomas; (2) pediatric-type diffuse low-grade gliomas; (3) pediatric-type diffuse high-grade gliomas (“HGG”); (4) circumscribed astrocytic gliomas; (5) glioneuronal and neuronal tumors; and (6) ependymomas.

In August 2021, we announced plans for treating pediatric brain cancer at the 2021 American Association of Neurological Surgeons Annual Scientific Meeting. In July 2021, we reported that we had received FDA feedback pertaining to a pre-IND meeting briefing package in which the FDA stated that we are not required to perform any additional preclinical or toxicology studies.

Since the initial FDA feedback and receiving important adult GBM data and experience with rhenium (<sup>186</sup>Re) obisbameda and follow-up communications with the FDA, we plan to submit a pediatric brain tumor investigational new drug application (“IND”) to investigate the use of rhenium (<sup>186</sup>Re) obisbameda in two pediatric brain cancers, high-grade glioma and ependymoma, in the first or second quarter of 2024.

Pediatric high-grade gliomas can be found almost anywhere within the CNS; however, they are most commonly found within the supratentorium. The highest incidence of supratentorial, high-grade gliomas in pediatrics appears to occur in children aged 15 to 19 years, with a median age of approximately nine years. Overall, pediatric high-grade glioma confers a three-year progression free survival (“PFS”) of  $11 \pm 3\%$  and three-year OS of  $22\% \pm 5\%$ . One-year PFS is as low as 40% in recent trials. Ependymomas are slow-growing central nervous system tumors that involve the ventricular system. Diagnosis is based on MRI and biopsy and survival rate depends on tumor grade and how much of the tumor can be removed. Grade II pathology was associated with significantly improved OS compared to Grade III (anaplastic) pathology (five-year OS =  $71 \pm 5\%$  vs.  $57 \pm 10\%$ ;  $p = 0.026$ ). Gross total resection compared to subtotal resection was associated with significantly improved OS (five-year OS =  $75 \pm 5\%$  vs.  $54 \pm 8\%$ ;  $p = 0.002$ ).

Overall, pediatric HGG and ependymoma are extremely difficult-to-treat pediatric brain tumors, frequently aggressive, and in recurrent settings, carry an extremely poor prognosis.

#### *Rhenium-188 NanoLiposome Biodegradable Alginate Microsphere Technology*

In January 2022, we announced that we licensed Biodegradable Alginate Microsphere (“BAM”) patents and technology from The University of Texas Health Science Center at San Antonio (“UTHSA”) to expand our tumor targeting capabilities and precision radiotherapeutics pipeline. We intend to combine our Rhenium NanoLiposome technology with the BAM technology to create a novel radioembolization technology. Initially, we intend to utilize the Rhenium-188 isotope, <sup>188</sup>RnL-BAM for the intra-arterial embolization and local delivery of a high dose of targeted radiation for a variety of solid organ cancers such as hepatocellular cancer, hepatic metastases, pancreatic cancer and many others.

Preclinical data from an *ex vivo* embolization experiment in which Technetium<sup>99m</sup>-BAM was intra-arterially delivered to a bovine kidney perfusion model was presented at the recent 2021 Society of Interventional Radiology Annual Scientific Meeting. The study concluded that the technology required for radiolabeling BAM could successfully deliver, embolize and retain radiation in the target organ. <sup>188</sup>RnL-BAM is a preclinical investigational drug we intend to further develop and move into clinical trials. Specifically, in 2022, we transferred the <sup>188</sup>RnL-BAM technology from UTHSA, and began planning to develop the drug product, and complete early preclinical studies to support a future FDA IND submission. Our intended initial clinical target is liver cancer which is the sixth most common and third deadliest cancer worldwide. It is a rare disease with increasing U.S. annual incidence (42,000) and deaths (30,000).

#### *Grant Agreement with CPRIT*

As noted above in the LM development discussion, on September 19, 2022, we entered into CPRIT Contract, effective as of August 31, 2022, with CPRIT, pursuant to which CPRIT will provide us the CPRIT Grant over a three-year period to fund the continued development of rhenium (<sup>186</sup>Re) obisbameda for the treatment of patients with LM. The CPRIT Grant is subject to customary CPRIT funding conditions, including, but not limited to, a matching fund requirement (one dollar from Plus Therapeutics for every two dollars awarded by CPRIT), revenue sharing obligations upon commercialization of rhenium (<sup>186</sup>Re) obisbameda based on specific dollar thresholds until CPRIT receives the aggregate amount of 400% of the proceeds awarded under the CPRIT Grant, and certain reporting requirements.

#### **Corporate Information**

We were initially formed as a California general partnership in July 1996, and subsequently incorporated in the State of Delaware in May 1997. 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](http://www.plustherapeutics.com). The contents of our website are not part of this prospectus and the references in this prospectus 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 to be Offered	Up to shares of common stock based on an assumed combined public offering price of \$ per share of common stock and accompanying common warrant, which is equal to the last sale price of our common stock as reported by Nasdaq on , 2024.
Pre-funded Warrants to be Offered	<p>We are also offering to those purchasers, if any, whose purchase of the common stock in this offering would result in the purchaser, together with its affiliates and certain related parties, beneficially owning more than 4.99% (or at the election of the purchaser, 9.99%) of our outstanding common stock immediately following the consummation of this offering, the opportunity to purchase, if they so choose, pre-funded warrants in lieu of the common stock that would otherwise result in ownership in excess of 4.99% (or 9.99%, as applicable) of our outstanding common stock.</p> <p>The purchase price of each pre-funded warrant will equal the price per share of common stock being sold to the public in this offering, minus \$0.001, and the exercise price of each pre-funded warrant will be \$0.001 per share.</p> <p>For each pre-funded warrant we sell, the number of shares of common stock we are offering will be decreased on a one-for-one basis. Because we will issue a common warrant for each share of our common stock and for each pre-funded warrant sold in this offering, the number of common warrants sold in this offering will not change as a result of a change in the mix of the shares of our common stock and pre-funded warrants sold.</p> <p>Each pre-funded warrant will be immediately exercisable and may be exercised at any time until exercised in full. There is no expiration date for the pre-funded warrants. To better understand the terms of the pre-funded warrants, you should carefully read the “Description of Capital Stock” section of this prospectus. You should also read the form of pre-funded warrant, which is filed as an exhibit to the registration statement that includes this prospectus.</p>
Common Warrants to be Offered	<p>Each share of our common stock and each pre-funded warrant to purchase one share of our common stock is being sold together with a common warrant to purchase one share of our common stock. Each common warrant will have an exercise price of \$ per share, will be immediately exercisable, and will expire on the five (5) year anniversary of the original issuance date.</p> <p>The shares of common stock and pre-funded warrants, and the accompanying common warrants, as the case may be, can only be purchased together in this offering but will be issued separately and will be immediately separable upon issuance. This prospectus also</p>

## Table of Contents

	relates to the offering of the shares of common stock issuable upon exercise of the common warrants.
Lock-Up Agreements	We and all of our executive officers and directors will enter into lock-up agreements with the placement agent. Under these agreements, we and each of these persons may not, without the prior written approval of the placement agent, offer, sell, contract to sell or otherwise dispose of or hedge common stock or securities convertible into or exchangeable for common stock, subject to certain exceptions. The restrictions contained in these agreements will be in effect for a period of forty-five days after the closing of this offering. For more information, see “Plan of Distribution.”
Placement Agent Warrants	We have agreed to issue to the placement agent or its designees as compensation in connection with this offering, the placement agent warrants to purchase up to 7.0% of the aggregate number of shares of common stock sold in this offering (including the shares of common stock issuable upon the exercise of the pre-funded warrants) at an exercise price equal to 125% of the combined public offering price per share and accompanying common warrant to be sold in this offering. The placement agent warrants will be exercisable upon issuance and will expire five (5) years from the commencement of sales under this offering.
Shares of our common stock outstanding prior to this offering (as of December 31, 2023)	4,444,097 shares of our common stock.
Shares of our common stock to be outstanding after this offering	shares of our common stock (assuming we sell only shares of common stock and no pre-funded warrants and assuming no exercise of the common warrants).
Use of proceeds	We intend to use the proceeds from this offering 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 11 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 4,444,097 shares outstanding as of December 31, 2023, and excludes, as of December 31, 2023:

- 140,109 shares of common stock issuable upon exercise of stock options outstanding under our equity incentive plans, with a weighted-average exercise price of \$37.48 per share;

[Table of Contents](#)

- 6,024 shares of common stock reserved for future issuance under our 2015 New Employee Incentive Plan;
- 180,607 shares of common stock reserved for future issuance under our 2020 Stock Incentive Plan;
- 398 and 27,792 shares of common stock issuable upon conversion of 1,014 shares of Series B Convertible Preferred Stock and 938 shares of Series C Preferred Stock, respectively;
- 142,733 shares of common stock issuable upon the exercise of warrants to purchase common stock, with a weighted-average exercise price of \$34.10 per share; and
- up to 1,423,319 shares of our common stock available to be sold as of March 7, 2024, pursuant to the Purchase Agreement under the prior registration statements, and an additional 1,300,000 shares of our common stock available to be sold in connection with the November 2023 registration statement that was declared effective on November 20, 2023.

## 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 for the fiscal year ended December 31, 2023, which is incorporated by reference in this prospectus, together with the information included in this prospectus and documents incorporated by reference herein, and in any free writing prospectus that we have authorized for use in connection with this offering. 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, as well as the value of the pre-funded warrants and common warrants, and you could lose all or part of your investment in our securities.*

### **Risks Related to the Offering**

***Our management has broad discretion over the use of the net proceeds from this offering, you may not agree with how we use the proceeds and the proceeds may not be invested successfully.***

Our management has broad discretion as to the use of the net proceeds from this offering, and we could use them for purposes other than those currently contemplated. Accordingly, you rely on the judgment of our management with regard to the use of those net proceeds, and you do not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. It is possible that 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.

***If you purchase our securities in this offering, you will incur immediate and substantial dilution in the book value of your shares of common stock.***

You will suffer immediate and substantial dilution in the net tangible book value of the common stock you purchase in this offering. Based on the assumed public offering price of \$ \_\_\_\_\_ per share, the last reported price of our common stock on the Nasdaq Capital Market on \_\_\_\_\_, 2024, purchasers of securities in this offering will experience immediate dilution of \$ \_\_\_\_\_ per share in net tangible book value of the common stock. See the section of this prospectus titled “*Dilution*” for a more detailed description of these factors.

***There is no public market for any pre-funded warrants or the common warrants being offered in this offering.***

There is no established public trading market for the pre-funded warrants or the common warrants being sold in this offering, and we do not expect a market to develop. We will not list the pre-funded warrants or the common warrants on any securities exchange or nationally recognized trading system, including the Nasdaq Capital Market. Without an active market, the liquidity of the pre-funded warrants and the common warrants will be limited.

***Purchasers who purchase our securities in this offering pursuant to a securities purchase agreement may have rights not available to purchasers that purchase without the benefit of a securities purchase agreement.***

In addition to rights and remedies available to all purchasers in this offering under federal securities and state law, purchasers that enter into a securities purchase agreement will also be able to bring claims of breach of contract against us. The ability to pursue a claim for breach of contract provides those investors with the means



## Table of Contents

to enforce the covenants uniquely available to them under the securities purchase agreement including: (i) timely delivery of shares; (ii) agreement to not enter into variable rate financings for \_\_\_\_\_ from closing, subject to certain exceptions; (iii) agreement to not enter into any financings for forty-five days from closing, subject to certain exceptions; and (iv) indemnification for breach of contract.

***This is a best efforts offering, with no minimum amount of securities required to be sold, and we may not raise the amount of capital we believe is required for our business plans, including our near-term business plans, nor will investors in this offering receive a refund in the event that we do not sell an amount of securities sufficient to pursue the business goals outlined in this prospectus.***

The placement agent has agreed to use its reasonable best efforts to solicit offers to purchase the securities in this offering. The placement agent has no obligation to buy any of the securities from us or to arrange for the purchase or sale of any specific number or dollar amount of the securities. We may sell fewer than all of the securities offered hereby, which may significantly reduce the amount of proceeds received by us, and investors in this offering will not receive a refund in the event that we do not sell an amount of securities sufficient to support our business goals, continued operations, including our near-term continued operations. Thus, we may not raise the amount of capital we believe is required for our operations in the short-term and may need to raise additional funds to complete such short-term operations. Such additional fundraises may not be available or available on terms acceptable to us, or at all.

There is no required minimum number of securities that must be sold as a condition to completion of this offering, and we have not, nor will we, establish an escrow account in connection with this offering. Because there is no minimum offering amount required as a condition to the closing of this offering, the actual offering amount, placement agent fees and proceeds to us are not presently determinable and may be substantially less than the maximum amounts set forth herein. Because there is no escrow account and no minimum offering amount, investors could be in a position where they have invested in us, but we are unable to fulfill our objectives due to a lack of interest in this offering. Further, because there is no escrow account in operation and no minimum investment amount, any proceeds from the sale of securities offered by us will be available for our immediate use, despite uncertainty about whether we would be able to use such funds to effectively implement our business plan. Investor funds will not be returned under any circumstances whether during or after the offering.

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

The pre-funded warrants and common warrants do not confer any rights of common stock ownership on their holders, such as voting rights or the right to receive dividends, but merely represent the right to acquire shares of common stock at a fixed price. Commencing on the date of issuance, holders of pre-funded warrants or common warrants may exercise their right to acquire the underlying common stock and pay the stated warrant exercise price per share.

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

***Raising additional capital may cause dilution to our stockholders, including purchasers of securities in this offering, restrict our operations or require us to relinquish rights to our technologies or current or future therapeutic candidates.***

Until such time, if ever, as we can generate the cash we need from operations, we expect to finance our cash needs through a combination of private and public equity offerings, debt financings, collaborations, strategic

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## [Table of Contents](#)

alliances and marketing, distribution or licensing arrangements. To the extent that we raise additional capital through the sale of common stock or securities convertible into or exchangeable for common stock, the ownership interest of our shareholders will be diluted, and the terms of these new securities may include liquidation or other preferences that materially adversely affect the rights of our shareholders. Debt financing, if available, would increase our fixed payment obligations and may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third-parties, we may have to relinquish valuable rights to our intellectual property, future revenue streams, research programs or current or future therapeutic candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds when needed, we may be required to delay, scale back or discontinue the development and commercialization of one or more of our therapeutic candidates, delay our pursuit of potential licenses or acquisitions, or grant rights to develop and market current or future therapeutic candidates that we would otherwise prefer to develop and market ourselves.

In addition, we have a significant number of stock options, convertible preferred stock and warrants to purchase shares of our common stock outstanding. To the extent that outstanding stock options, convertible preferred stock or warrants have been or may be exercised or other shares issued, you may experience dilution.

## 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 (the “Securities Act”), and Section 21E of the Securities Exchange Act of 1934, as amended (the “Exchange Act”). Statements other than statements of historical fact, which address activities, events or developments that we “intend,” “expect,” “believe,” “anticipate,” “will,” “should,” “would,” “could,” “may,” “designed,” “potential,” “evaluate,” “progressing,” “proceeding,” “exploring,” “hopes,” and similar expressions, or future conditional verbs such as “will,” “should,” “would,” “could” or “may” occur in the future are forward looking statements. 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, and general and administrative expenses; our strategic collaborations and license agreements, intellectual property, U.S. Food and Drug Administration and European Medicines Agency approvals and interactions and government regulation; the potential size of the market for our product candidates; our research and development efforts; results from our pre-clinical and clinical studies and the implications of such results regarding the efficacy or safety of our product candidates; the safety profile, pathways, and efficacy of our product candidates and formulations; anticipated advantages of our product candidates over other products available in the market and being developed; the populations that will most benefit from our product candidates and indications that will be pursued with each product candidate; anticipated progress in our current and future clinical trials; plans and strategies to create novel technologies; our IP strategy; competition future development and/or expansion of our product candidates and therapies in our markets; sources of competition for any of our product candidates; our pipeline; our ability to generate product or development revenues and the sources of such revenue; 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 Report on Form 10-K for the year ended December 31, 2023, filed with the SEC on March 5, 2024; our ability to fully access our equity line with Lincoln Park; our need for additional financing and the availability thereof; 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 ability to transfer the drug product manufacture to a contract drug manufacturing organization; the potential enhancement of our cash position through development, marketing, and licensing arrangements; potential enhancement of our cash position through development, marketing, and licensing arrangements; and a material security breach or cybersecurity attack affecting our operations and property.

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, 2023, which is incorporated herein by reference. 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.

## USE OF PROCEEDS

We estimate that the net proceeds that we will receive from the sale of our common stock and accompanying common warrants in this offering will be approximately \$ \_\_\_\_\_ million, after deducting placement agent's fees and other offering expenses payable by us, assuming a public offering price of \$ \_\_\_\_\_ per share and accompanying common warrant, which is the last reported sale price of our common stock on Nasdaq Capital Market on \_\_\_\_\_, 2024, assuming no sale of pre-funded warrants and excluding the proceeds, if any, from the exercise of any common warrants issued in this offering.

We expect to use any proceeds that we receive from this offering 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. We cannot specify with certainty all of the particular uses for the net proceeds that we will have from the offering. 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.

## DILUTION

If you invest in our securities in this offering, your ownership interest may be diluted immediately to the extent of the difference between the public offering price per share of our common stock and accompanying common warrant and the as adjusted net tangible book value per share of our common stock immediately after this offering.

Our historical net tangible book value as of December 31, 2023, was \$(1.8) million, or \$(0.40) per share of our outstanding common stock. Our historical net tangible book value represents the amount of our total tangible assets less our total liabilities. Historical net tangible book value per share represents historical net tangible book value divided by the number of shares of our common stock outstanding as of December 31, 2023.

After giving effect to the sale of shares of our common stock and common warrants to purchase up to shares of our common stock in this offering at an assumed public offering price of \$ \_\_\_\_\_ per share (which was the last reported sale price of our common stock on Nasdaq on March \_\_\_\_\_, 2024, and accompanying common warrant, assuming no sale of any pre-funded warrants, and after deducting placement agent fees and estimated offering expenses payable by us, our as adjusted net tangible book value as of December 31, 2023 would have been \$ \_\_\_\_\_ million, or \$ \_\_\_\_\_ per share. This represents an immediate increase in as adjusted net tangible book value of \$ \_\_\_\_\_ per share to our existing stockholders and an immediate dilution of \$ \_\_\_\_\_ per share to investors purchasing our common stock and common warrants in this offering at the assumed combined public offering price. The final public offering price will be determined through negotiation between us, the placement agent and the investors in the offering and may be at a discount to the current market price. Therefore, the assumed public offering price used throughout this prospectus may not be indicative of the final public offering price.

The following table illustrates this dilution on a per share basis:

Assumed combined public offering price per share of common stock and accompanying common warrant		\$
Historical net tangible book value per share as of December 31, 2023	\$(0.40)	—
Increase in net tangible book value per share as of December 31, 2023 attributable to investors purchasing shares in this offering		—
As adjusted net tangible book value per share as of December 31, 2023 after giving effect to this offering		( )
Dilution per share to investors participating in this offering		\$ _____

Each \$1.00 increase or decrease in the assumed public offering price of \$ \_\_\_\_\_ per share, the last reported sale price of our common stock on the Nasdaq on \_\_\_\_\_, 2024, would increase or decrease our as adjusted net tangible book value per share after this offering by \$ \_\_\_\_\_ per share. For each \$ \_\_\_\_\_ increase or decrease in the assumed public offering price, the dilution per share to investors participating in this offering would increase or decrease by \$ \_\_\_\_\_ per share, assuming that the number of shares of common stock offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting placement agent fees and commissions and estimated offering expenses payable by us. Similarly, an increase of shares of common stock offered by us would increase the as adjusted net tangible book value after this offering by \$ \_\_\_\_\_ per share and decrease the dilution per share to investors participating in this offering by \$ \_\_\_\_\_ per share, and a decrease of shares of common stock offered by us would decrease the as adjusted net tangible book value by \$ \_\_\_\_\_ per share and increase the dilution per share to investors in this offering by \$ \_\_\_\_\_ per share, assuming that the assumed public offering price remains the same, and after deducting placement agent fees and estimated offering expenses payable by us.

## [Table of Contents](#)

Unless otherwise noted, the number of shares of common stock to be outstanding immediately after this offering in the table above is based on 4,444,097 shares outstanding as of December 31, 2023, and excludes, as of December 31, 2023:

- 140,109 shares of common stock issuable upon exercise of stock options outstanding under our equity incentive plans, with a weighted-average exercise price of \$37.48 per share;
- 6,024 shares of common stock reserved for future issuance under our 2015 New Employee Incentive Plan;
- 180,607 shares of common stock reserved for future issuance under our 2020 Stock Incentive Plan;
- 398 and 27,792 shares of common stock issuable upon conversion of 1,014 shares of Series B Convertible Preferred Stock and 938 shares of Series C Preferred Stock, respectively;
- 142,733 shares of common stock issuable upon the exercise of warrants to purchase common stock, with a weighted-average exercise price of \$34.10 per share; and
- up to 1,423,319 shares of our common stock available to be sold as of November 21, 2023, pursuant to the Purchase Agreement under the August 2023 registration statement, and an additional 1,300,000 shares of our common stock available under the November 2023 registration statement that was declared effective on November 20, 2023, is declared effective.

## 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.” On \_\_\_\_\_, 2024, the closing price as reported on Nasdaq Capital Market of our common stock was \$ \_\_\_\_\_ per share. There is no established public trading market for the pre-funded warrants or the common warrants, and we do not expect a market to develop. In addition, we do not intend to apply for a listing of the pre-funded warrants or the common warrants on any national securities exchange.

### Holders

As of March 8, 2024, there were approximately 4 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. In addition, the terms of our loan agreement with Oxford Finance, LLC preclude us from paying dividends. Investors should not purchase our common stock with the expectation of receiving cash dividends.

## 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 (the "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, our amended and restated bylaws and the applicable provisions of the DGCL for additional information before you buy any of our securities. See "Where You Can Find More Information."*

### Common Stock

We are authorized to issue 100,000,000 shares of common stock. As of December 31, 2023, there were 4,444,097 shares of our common stock issued and outstanding. Each holder of our 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, 1,952 shares of which were issued and outstanding as of December 31, 2023. Of this amount, (i) 13,500 shares have been designated as Series A Convertible Preferred Stock, 0 shares of which are outstanding, (ii) 10,000 shares have been designated as Series B Convertible Preferred Stock, 1,014 shares of which are outstanding, (iii) 7,000 shares have been designated Series C Convertible Preferred Stock, 938 shares of which are outstanding and (iv) 1 share has been designated as Series F Preferred Stock, of which there are no shares outstanding, in each case, as of December 31, 2023.

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;



## Table of Contents

- any preferential amount payable upon shares of the series in the event of the liquidation, dissolution or winding up of, or upon the distribution of any of our assets; and
- the prices or rates of conversion or exchange at which, and the terms and conditions on which, the shares of the series may be converted or exchanged into other securities, if the shares are convertible or exchangeable.

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

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

### ***Series B Preferred Stock***

*Conversion.* Each share of Series B Preferred Stock is convertible, at our option or at the option of the holder, at any time, into the number of shares of our common stock determined by dividing the \$1,000 stated value per share of the Series B Preferred Stock by a conversion price of \$2,547.74 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 is convertible, at our option at any time, 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 \$33.75. 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 does not have the right to convert any portion of the Series C Preferred Stock to the extent that, after giving effect to the conversion, the holder, together with its affiliates, would beneficially own in excess of 9.99% of the number of shares of our common stock outstanding immediately after giving effect to its conversion.

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

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

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

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

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

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

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

Certain provisions of Delaware law, our amended and restated certificate of incorporation, as amended, and our amended and restated bylaws could have the effect of delaying, deferring or discouraging another party from acquiring control of us. These provisions, which are summarized below, are expected to discourage certain types of coercive takeover practices and inadequate takeover bids. These provisions are also designed, in part, to encourage persons seeking to acquire control of us to first negotiate with our board of directors.

## [Table of Contents](#)

*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 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

## [Table of Contents](#)

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.

### **Anti-Takeover Effects of Provisions of Our Certificate of Incorporation, Our Bylaws and Delaware Law**

Some provisions of Delaware law, our amended and restated certificate of incorporation and our amended and restated bylaws contain provisions that could make hostile takeovers, including the following transactions, more difficult: an acquisition of us by means of a tender offer; an acquisition of us by means of a proxy contest or otherwise; or the removal of our incumbent officers and directors. 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 the composition of our board and management. It is possible that these provisions could make it more difficult to accomplish or could deter transactions that stockholders may otherwise consider to be in their best interest or in our best interests, including transactions which provide for payment of a premium over the market price for our shares.

These provisions, summarized below, are intended to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our Board. We believe that the benefits of the increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure us outweigh the disadvantages of discouraging these proposals because negotiation of these proposals could result in an improvement of their terms.

#### *Delaware Anti-Takeover Statute*

We are subject to Section 203 of the DGCL, which prohibits persons deemed to be “interested stockholders” from engaging in a “business combination” with a publicly held Delaware corporation for three years following the date these persons become interested stockholders unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies. Generally, 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 voting stock. Generally, a “business combination” includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. The existence of this provision may have an anti-takeover effect with respect to transactions not approved in advance by the board of directors. A Delaware corporation may “opt out” of these provisions with an express provision in its original certificate of incorporation or an express provision in its certificate of incorporation or bylaws resulting from a stockholders’ amendment approved by at least a majority of the outstanding voting shares. We have not opted out of these provisions. As a result, mergers or other takeover or change in control attempts of us may be discouraged or prevented.

#### *Undesignated Preferred Stock*

The ability of our Board, without action by the stockholders, to issue undesignated shares of preferred stock with voting or other rights or preferences as designated by our Board could impede the success of any attempt to change control of us. These and other provisions may have the effect of deferring hostile takeovers or delaying changes in control or management of our company.

#### *Authorized Common Stock*

Our authorized but unissued shares of common stock will be available for future issuance without stockholder approval. These additional shares may be utilized for a variety of corporate purposes, including

## [Table of Contents](#)

future public offerings to raise additional capital and corporate acquisitions. The existence of authorized but unissued shares of common stock could render more difficult or discourage an attempt to obtain control of a majority of our common stock by means of a proxy contest, tender offer, merger or otherwise.

### *Advance Notice Requirements for Stockholder Proposals and Director Nominations*

Our amended and restated bylaws will provide advance notice procedures for stockholders seeking to bring business before our annual meeting of stockholders, or to nominate candidates for election as directors at any meeting of stockholders. Our amended and restated bylaws also will specify certain requirements regarding the form and content of a stockholder's notice. These provisions may preclude our stockholders from bringing matters before our annual meeting of stockholders or from making nominations for directors at our meetings of stockholders.

### *No Cumulative Voting; No Action Without a Meeting; Special Meeting of Stockholders*

Stockholders will not be permitted to cumulate their votes for the election of directors. In addition, stockholders will not be able to take action by written consent and will only be able to take action at annual or special meetings of our stockholders. Furthermore, special meetings of our stockholders may be called only by our Chief Executive Officer, our President, our Board or its Chairman.

### *Exclusive Forum Selection*

Our amended and restated bylaws require, to the fullest extent permitted by law, subject to limited exceptions, that derivative actions brought in our name, actions against directors, officers and employees for breach of fiduciary duty and other similar actions may be brought only in the Court of Chancery in the State of Delaware and, if brought outside of Delaware, the stockholder bringing the suit will be deemed to have consented to service of process on such stockholder's counsel in any action brought to enforce the exclusive forum provision. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and consented to the forum provisions in our amended and restated bylaws.

Our amended and restated bylaws further provide that unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States will be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act and the respective rules and regulations promulgated thereunder.

### **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."

## DESCRIPTION OF SECURITIES WE ARE OFFERING

The following is a summary of the material terms of our common stock. For additional information about our authorized capital, including our common stock, our outstanding warrants to purchase common stock, and convertible preferred stock, we refer you to our amended and restated certificate of incorporation and amended and restated bylaws, which are included herein as Exhibit 3.1, Exhibit 3.2, Exhibit 3.3, Exhibit 3.4, Exhibit 3.5, Exhibit 3.6, and 3.10, respectively, and our filings with the SEC that are incorporated by reference in this prospectus, including our Annual Report on Form 10-K for the year ended December 31, 2023. For instructions on how to find copies of these documents, please read “Where You Can Find Additional Information” and “Information Incorporated by Reference.”

### Common Stock

The material terms and provisions of our common stock and each other class of our securities which qualifies or limits our common stock are described under the caption “Description of Capital Stock” in this prospectus.

### Common Warrants

The following summary of certain terms and provisions of the common warrants that are being offered hereby is not complete and is subject to, and qualified in its entirety by, the provisions of the Common Warrant, the form of which will be filed as an exhibit to the registration statement of which this prospectus forms a part. Prospective investors should carefully review the terms and provisions of the form of common warrant for a complete description of the terms and conditions of the common warrants.

#### *Duration, Exercise Price and Form*

Each common warrant offered hereby will have an exercise price equal to \$ \_\_\_\_\_ per share. The common warrants will be immediately exercisable and may be exercised until the five year anniversary of the original issuance date. The exercise price and number of shares of common stock issuable upon exercise is subject to appropriate adjustment in the event of stock dividends, stock splits, reorganizations or similar events affecting our common stock and the exercise price. The common warrants will be issued separately from the common stock or the pre-funded warrants, as the case may be, and may be transferred separately immediately thereafter. The common warrants will be issued in certificated form only.

#### *Exercisability*

The common warrants will be exercisable, at the option of each holder, in whole or in part, by delivering to us a duly executed exercise notice accompanied by payment in full for the number of shares of our common stock purchased upon such exercise (except in the case of a cashless exercise as discussed below). A holder (together with its affiliates) may not exercise any portion of such holder’s warrants to the extent that the holder would own more than 4.99% of the outstanding common stock (or at the election of a holder prior to the date of issuance, 9.99%) immediately after exercise, except that upon prior notice from the holder to us, the holder may increase or decrease such beneficial ownership limitation, provided that in no event shall the beneficial ownership limitation exceed 9.99% and any increase in the beneficial ownership limitation will not be effective until sixty-one days following notice of such increase from the holder to us.

#### *Cashless Exercise*

If at the time of exercise there is no effective registration statement registering our common stock underlying the common warrants, or the prospectus contained therein is not available for the issuance of the underlying shares to the holder, in lieu of making the cash payment otherwise contemplated to be made to us upon such exercise in payment of the aggregate exercise price, the holder may elect instead to receive upon such exercise (either in whole or in part) the net number of shares of common stock determined according to a formula set forth in the common warrant.

## Table of Contents

### *Fundamental Transactions*

In the event of a fundamental transaction, as described in the common warrants and generally including any reorganization, recapitalization or reclassification of our common stock, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, the acquisition of more than 50% of our outstanding common stock, or any person or group becoming the beneficial owner of more than 50% of the voting power represented by our outstanding common stock, the holders of the common warrants will be entitled to receive upon exercise of the common warrants the kind and amount of securities, cash or other property that the holders would have received had they exercised the common warrants immediately prior to such fundamental transaction. In addition, in certain circumstances, upon a fundamental transaction, the holder of a common warrant will have the right to require us to repurchase its common warrants at the Black-Scholes value; provided, however, that, if the fundamental transaction is not within our control, including not approved by our Board, then the holder will only be entitled to receive the same type or form of consideration (and in the same proportion), at the Black-Scholes value of the unexercised portion of the common warrant that is being offered and paid to the holders of our common stock in connection with the fundamental transaction.

### *Transferability*

Subject to applicable laws, a common warrant may be transferred at the option of the holder upon surrender of the common warrant to us together with the appropriate instruments of transfer.

### *Fractional Shares*

No fractional shares of common stock will be issued upon the exercise of the common warrants. Rather, the number of shares of common stock to be issued will, at our election, either be rounded up to the nearest whole number or we will pay a cash adjustment in respect of such final fraction in an amount equal to such fraction multiplied by the exercise price.

### *Trading Market*

There is no established trading market for the common warrants, and we do not expect a market to develop. We do not intend to apply for a listing of the common warrants on any securities exchange or other nationally recognized trading system. Without an active trading market, the liquidity of the common warrants will be limited. The common stock issuable upon exercise of the common warrants is currently listed on Nasdaq.

### *Rights as a Stockholder*

Except as otherwise provided in the common warrants or by virtue of the holders' ownership of shares of common stock, the holders of the common warrants do not have the rights or privileges of holders of our shares of common stock, including any voting rights, until such common warrant holders exercise their common warrants.

### *Waivers and Amendments*

No term of the common warrants may be amended or waived without the written consent of the holders of the common warrants purchased in this offering.

### **Pre-Funded Warrants**

The following summary of certain terms and provisions of the pre-funded warrants that are being offered hereby is not complete and is subject to, and qualified in its entirety by, the provisions of the pre-funded warrant, the form of which will be filed as an exhibit to the registration statement of which this prospectus forms a part. Prospective investors should carefully review the terms and provisions of the form of pre-funded warrant for a complete description of the terms and conditions of the pre-funded warrants.

## Table of Contents

### *Duration, Exercise Price and Form*

The pre-funded warrants offered hereby will have an exercise price of \$0.001 per share. The pre-funded warrants will be immediately exercisable and may be exercised at any time after their original issuance until such pre-funded warrants are exercised in full. The exercise price and number of shares of common stock issuable upon exercise are subject to appropriate adjustment in the event of share dividends, share splits, reorganizations or similar events affecting our shares of common stock. The pre-funded warrants and common warrants are immediately separable and will be issued separately in this offering, but must be purchased together in this offering. The pre-funded warrants will be issued in certificated form only.

### *Exercisability*

The pre-funded warrants will be exercisable, at the option of each holder, in whole or in part, by delivering to us a duly executed exercise notice accompanied by payment in full for the number of shares of our common stock purchased upon such exercise (except in the case of a cashless exercise as discussed below). A holder (together with its affiliates) may not exercise any portion of the pre-funded warrants to the extent that the holder would own more than 4.99% (or at the election of a holder prior to the date of issuance, 9.99%) of the outstanding common stock immediately after exercise; provided, however, that upon prior notice to us, the holder may increase or decrease such beneficial ownership limitation, provided that in no event shall the beneficial ownership limitation exceed 9.99% and any increase in the beneficial ownership limitation will not be effective until sixty-one days following notice of such increase from the holder to us.

### *Cashless Exercise*

At the time a holder exercises its pre-funded warrants, in lieu of making the cash payment otherwise contemplated to be made to us upon such exercise in payment of the aggregate exercise price, the holder may elect instead to receive upon such exercise (either in whole or in part) the net number of shares of common stock determined according to a formula set forth in the pre-funded warrants.

### *Fundamental Transactions*

In the event of a fundamental transaction, as described in the pre-funded warrants and generally including any reorganization, recapitalization or reclassification of our common stock, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, the acquisition of more than 50% of our outstanding common stock, or any person or group becoming the beneficial owner of more than 50% of the voting power represented by our outstanding common stock, the holders of the pre-funded warrants will be entitled to receive upon exercise of the pre-funded warrants the kind and amount of securities, cash or other property that the holders would have received had they exercised the pre-funded warrants immediately prior to such fundamental transaction.

### *Transferability*

Subject to applicable laws, a pre-funded warrant may be transferred at the option of the holder upon surrender of the pre-funded warrant to us together with the appropriate instruments of transfer.

### *Fractional Shares*

No fractional shares of common stock will be issued upon the exercise of the pre-funded warrants. Rather, the number of shares of common stock to be issued will, at our election, either be rounded up to the nearest whole number or we will pay a cash adjustment in respect of such final fraction in an amount equal to such fraction multiplied by the exercise price.



## Table of Contents

### *Trading Market*

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

### *Rights as a Stockholder*

Except as otherwise provided in the pre-funded warrants or by virtue of the holders' ownership of shares of common stock, the holders of pre-funded warrants do not have the rights or privileges of holders of our shares of common stock, including any voting rights, until such pre-funded warrants holders exercise their warrants.

### *Waivers and Amendments*

No term of the pre-funded warrants may be amended or waived without the written consent of the holders of the pre-funded warrants purchased in this offering.

### **Placement Agent Warrants**

We have also agreed to issue to the placement agent or its designees, placement agent warrants as compensation in connection with this offering to purchase up to \_\_\_\_\_ shares of common stock as compensation in connection with this offering. The placement agent warrants will be exercisable immediately and will have substantially the same terms as the common warrants described above, except that the placement agent warrants will have an exercise price of \$ \_\_\_\_\_ per share (representing 125% of the offering price per share and accompanying common warrant) and a termination date that will be five years from the commencement of the sales pursuant to this offering. See "Plan of Distribution" below.

## PLAN OF DISTRIBUTION

Pursuant to that certain engagement agreement (the “Engagement Agreement”), we have engaged \_\_\_\_\_, or the placement agent, to act as our exclusive placement agent to solicit offers to purchase the shares of our common stock, pre-funded warrants and common warrants offered by this prospectus. The placement agent is not purchasing or selling any such securities, nor is it required to arrange for the purchase and sale of any specific number or dollar amount of such securities, other than to use its “reasonable best efforts” to arrange for the sale of such securities by us. Therefore, we may not sell all of the shares of common stock, pre-funded warrants and common warrants being offered. The terms of this offering are subject to market conditions and negotiations between us, the placement agent and prospective investors. The placement agent will have no authority to bind us by virtue of the Engagement Agreement. This is a best efforts offering and there is no minimum offering amount required as a condition to the closing of this offering. The placement agent may retain sub-agents and selected dealers in connection with this offering.

Investors purchasing securities offered hereby will have the option to execute a securities purchase agreement with us. Investors who do not enter into a securities purchase agreement shall rely solely on this prospectus in connection with the purchase of our securities in this offering. In addition to rights and remedies available to all purchasers in this offering under federal securities and state law, the purchasers which enter into a securities purchase agreement will also be able to bring claims of breach of contract against us. The ability to pursue a claim for breach of contract is material to larger purchasers in this offering as a means to enforce the following covenants uniquely available to them under the securities purchase agreement, including but not limited to: (i) a covenant to not enter into variable rate financings for a period of \_\_\_\_\_ following the closing of the offering, subject to exceptions; and (ii) a covenant to not enter into any equity financings for forty five-days from closing of the offering, subject to certain exceptions.

The nature of the representations, warranties and covenants in the securities purchase agreements shall include, but are not limited to:

- standard issuer representations and warranties on matters such as organization, qualification, authorization, no conflict, no governmental filings required, current in SEC filings, no litigation, labor or other compliance issues, environmental, intellectual property and title matters and compliance with various laws such as the Foreign Corrupt Practices Act; and
- covenants regarding matters such as registration of shares issued and issuable upon exercise of the common stock purchase warrants, no integration with other offerings, no shareholder rights plans, use of proceeds, indemnification of purchasers, reservation and listing of common stock, and no subsequent equity sales for a period of forty five-days, subject to certain exceptions.

Delivery of the shares of common stock, pre-funded warrants and common warrants offered hereby is expected to occur on or about \_\_\_\_\_, 2024, subject to satisfaction of certain customary closing conditions.

### Fees and Expenses

The following table shows the per share and common warrant and per pre-funded warrant and common warrant and total placement agent fees we will pay in connection with the sale of the securities in this offering.

	<u>Per Share and Common Warrant</u>	<u>Per Pre-Funded Warrant and Common Warrant</u>	<u>Total</u>
Public offering price			
Placement agent fees			
Proceeds to us (before expenses)			

## Table of Contents

We have agreed to pay the placement agent a total cash fee equal to 7.0% of the aggregate gross proceeds raised in the offering and a management fee equal to 1.0% of the gross proceeds raised in this offering. We will also pay the placement agent a non-accountable expense allowance of \$50,000, its legal fees and expenses in an amount up to \$100,000 and its clearing fees in an amount up to \$15,950 in connection with this offering. We estimate the total offering expenses of this offering that will be payable by us, excluding the placement agent fees and expenses, will be approximately \$

### **Placement Agent Warrants**

In addition, we have agreed to issue to the placement agent or its designees warrants, or the placement agent warrants, as compensation with this offering, to purchase up to 7.0% of the aggregate number of shares of common stock sold in this offering (including shares underlying any pre-funded warrants), at an exercise price equal to 125% of the public offering price per share and accompanying Common Warrant to be sold in this offering. The placement agent warrants will be exercisable upon issuance and will expire five years from the commencement of sales under this offering. The placement agent warrants and underlying shares of common stock are registered on the registration statement of which this prospectus is a part. The form of the placement agent warrant will be included as an exhibit to this registration statement of which this prospectus forms a part.

### **Tail**

In the event that any investors that were introduced to the Company by the placement agent or had back and forth correspondence with the placement agent with respect to a public offering or were brought over-the-wall by the placement agent with respect to a non-public offering, in each case during the term of our Engagement Agreement, provide any capital to us in a public or private offering or capital-raising transaction within nine (9) months following the termination or expiration of our Engagement Agreement with the placement agent, we shall pay the placement agent the cash and warrant compensation provided above on the gross proceeds from such investors, subject to certain exceptions.

### **Right of First Refusal**

If, from the date of the Engagement Agreement until the nine-month anniversary following consummation of each offering of our securities during the term of the Engagement Agreement, we or any of our subsidiaries decides to raise funds by means of a public offering (excluding an at-the-market facility) or a private placement or any other capital-raising financing of equity, equity-linked or debt securities, the placement agent (or any affiliate designated by the placement agent) shall have the right to act as sole book-running manager, sole underwriter or sole placement agent for such financing, subject to certain exceptions. If the placement agent or one of its affiliates decides to accept any such engagement, the agreement governing such engagement will contain, among other things, provisions for customary fees for transactions of similar size and nature and the provisions of the Engagement Agreement, including indemnification, which are appropriate to such a transaction.

### **Lock-Up Agreements**

Our officers and directors, representing beneficial ownership of 2.97% of our outstanding shares of common stock as of March 8, 2024, have agreed with the placement agent to be subject to a lock-up period of forty-five days following the closing of this offering. This means that, during the applicable lock-up period, such persons may not offer for sale, contract to sell, sell, distribute, grant any option, right or warrant to purchase, pledge, hypothecate or otherwise dispose of, directly or indirectly, any shares of our common stock or any securities convertible into, or exercisable or exchangeable for, shares of our common stock. Certain limited transfers are permitted during the lock-up period if the transferee agrees to these lock-up restrictions. We have also agreed to similar lock-up restrictions on the issuance and sale of our securities for forty-five days following the closing of this offering, subject to certain exceptions. The placement agent may, in its sole discretion and without notice, waive the terms of any of these lock-up agreements.

## [Table of Contents](#)

In addition, subject to certain exceptions, we have agreed to not issue any securities that are subject to a price reset based on the trading prices of our common stock or upon a specified or contingent event in the future, or enter into any agreement to issue securities at a future determined price for a period of \_\_\_\_\_ following the closing date of this offering, subject to an exception. The placement agent may, in its sole discretion and without notice, waive the terms of this prohibition.

### **Indemnification**

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

In addition, we will indemnify the purchasers of securities in this offering against liabilities arising out of or relating to (i) any breach of any of the representations, warranties, covenants or agreements made by us in the securities purchase agreement or related documents, or (ii) any action instituted against a purchaser by a third party (other than a third party who is affiliated with such purchaser) with respect to the securities purchase agreement or related documents and the transactions contemplated thereby, subject to certain exceptions.

### **Regulation M Compliance**

The placement agent may be deemed to be an underwriter within the meaning of Section 2(a)(11) of the Securities Act, and any fees received by it and any profit realized on the sale of our securities offered hereby by it while acting as principal might be deemed to be underwriting discounts or commissions under the Securities Act. The placement agent will be required to comply with the requirements of the Securities Act and the Exchange Act, including, without limitation, Rule 10b-5 and Regulation M under the Exchange Act. These rules and regulations may limit the timing of purchases and sales of our securities by the placement agent. Under these rules and regulations, the placement agent may not (i) engage in any stabilization activity in connection with our securities; and (ii) bid for or purchase any of our securities or attempt to induce any person to purchase any of our securities, other than as permitted under the Exchange Act, until they have completed their participation in the distribution.

### **Other Relationships**

The placement agent and its affiliates have engaged, and may in the future engage, in investment banking transactions and other commercial dealings in the ordinary course of business with us or our affiliates. The placement agent has received, or may in the future receive, customary fees and commissions for these transactions.

In addition, in the ordinary course of their business activities, the placement agent and its affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) for their own account and for the accounts of their customers. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The placement agent and its affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Except as disclosed in this prospectus, we have no present arrangements with the placement agent for any further services.

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[Table of Contents](#)

**Electronic Distribution**

A prospectus in electronic format may be made available on a website maintained by the placement agent and the placement agent may distribute prospectuses electronically. Other than the prospectus in electronic format, the information on these websites is not part of this prospectus or the registration statement of which this prospectus forms a part, has not been approved and/or endorsed by us or the placement agent and should not be relied upon by investors.

**Nasdaq listing**

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 Hogan Lovells US LLP, is acting as counsel for the placement agent in connection with this offering.

## EXPERTS

The financial statements of Plus Therapeutics, Inc. (the “Company”) as of December 31, 2023 and 2022 and for the years then ended incorporated by reference in this Prospectus have been so incorporated in reliance on the report of BDO USA P.C., an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting. The report on the financial statements contains an explanatory paragraph regarding the Company’s ability to continue as a going concern.

## 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](http://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. We also maintain a website at <https://plustherapeutics.com>. You may access our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, Proxy Statements and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act with the SEC free of charge at our website as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. Information contained in, or accessible through, our website is not a part of this prospectus, and the inclusion of our website address in this prospectus is only as an inactive textual reference.

## 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](#) for the year ended December 31, 2023, filed with the SEC on March 5, 2024; and
- 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 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](http://www.sec.gov) or on the “Investors” page of our website at [www.plustherapeutics.com](http://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.

Up to [\_\_\_\_\_] Shares of Common Stock



Pre-Funded Warrants to purchase up to \_\_\_\_\_ Shares of Common Stock

Common Warrants to purchase up to \_\_\_\_\_ Shares of Common Stock

\_\_\_\_\_ Shares of Common Stock underlying Pre-Funded Warrants and Common Warrants

Placement Agent Warrants to Purchase up to \_\_\_\_\_ Shares of Common Stock

\_\_\_\_\_ Shares of Common Stock Underlying the Placement Agent Warrants

\_\_\_\_\_  
**PRELIMINARY  
PROSPECTUS**  
\_\_\_\_\_

, 2024

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

The following table sets forth the estimated costs and expenses in connection with the offering described in this registration statement. All expenses incurred with respect to the sale and distribution of the securities being registered hereby (other than placement agent fees) will be borne by us. All amounts are estimates except the SEC registration fee and the Financial Industry Regulatory Authority (“FINRA”) filing fee.

	<u>Amount</u>
SEC registration fee	\$ —
FINRA filing fee	\$ —
Accountant’s fees and expenses	\$ —
Legal fees and expenses	\$ —
Transfer agent’s fees and expenses	\$ —
Printing fees and expenses	\$ —
Miscellaneous	\$ —
Total expenses	<u>\$ —</u>

**Item 14. Indemnification of Directors and Officers.**

Section 102(b)(7) of the DGCL enables a corporation, in its certificate of incorporation or an amendment thereto, to eliminate or limit 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.

## Table of Contents

Our amended and restated certificate of incorporation, as amended, and amended and restated bylaws 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 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.

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 DGCL.

### **Item 15. Recent Sales of Unregistered Securities.**

During the past three years, we sold the following shares of common stock, preferred stock, promissory notes and warrants without registration under the Securities Act:

On September 15, 2023, we issued 53,381 unregistered shares to Biocept, Inc., the fair value of which was \$75,000. Such issuance was exempt from registration under 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.**

(a) The undersigned Registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by section 10(a)(3) of the Securities Act of 1933;

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the 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

## Table of Contents

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 in the initial distribution of the securities, the undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:
  - (i) Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;
  - (ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;
  - (iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and
  - (iv) Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.
- (b) 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.
- (c) The undersigned Registrant hereby undertakes that:
  - (1) For purposes of determining any liability under the Securities, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.

## Table of Contents

- (2) For the purpose of determining any liability under the Securities, each post-effective amendment that contains a form of prospectus 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.

### EXHIBIT INDEX

Exhibit Number	Exhibit Title	Filed with this Form S-1	Incorporated by Reference		
			Form	File No.	Date Filed
3.1	<a href="#">Composite Certificate of Incorporation.</a>		10-K	001-34375 Exhibit 3.1	03/11/2016
3.2	<a href="#">Certificate of Amendment to Amended and Restated Certificate of Incorporation.</a>		8-K	001-34375 Exhibit 3.1	05/10/2016
3.3	<a href="#">Certificate of Amendment to Amended and Restated Certificate of Incorporation.</a>		8-K	001-34375 Exhibit 3.1	05/23/2018
3.4	<a href="#">Certificate of Amendment to Amended and Restated Certificate of Incorporation.</a>		8-K	001-34375 Exhibit 3.1	07/29/2019
3.5	<a href="#">Certificate of Amendment to Amended and Restated Certificate of Incorporation.</a>		8-K	001-34375 Exhibit 3.1	08/06/2019
3.6	<a href="#">Certificate of Amendment to Amended and Restated Certificate of Incorporation.</a>		8-K	001-34375 Exhibit 3.1	4/28/2023
3.7	<a href="#">Certificate of Designation of Preferences, Rights and Limitations of Series B Convertible Preferred Stock.</a>		8-K	001-34375 Exhibit 3.1	11/28/2017
3.8	<a href="#">Certificate of Designation of Preferences, Rights and Limitations of Series C Convertible Preferred Stock.</a>		8-K	001-34375 Exhibit 3.1	07/25/2018
3.9	<a href="#">Certificate of Designation of Series F Convertible Preferred Stock</a>		8-K	001-34375 Exhibit 3.1	03/03/2023
3.10	<a href="#">Amended and Restated Bylaws of Plus Therapeutics, Inc.</a>		8-K	001-34375 Exhibit 3.2	09/21/2021
4.1	<a href="#">Description of Securities.</a>		10-K	001-34375 Exhibit 4.1	03/30/2020
4.2	<a href="#">Form of Common Stock Certificate.</a>		10-K	001-34375 Exhibit 4.33	03/09/2018
4.3	<a href="#">Form of Series U Warrant.</a>		S-1/A	333-229485 Exhibit 4.37	09/16/2019
4.4	<a href="#">Form of Warrant Amendment Agreement.</a>		8-K	011-34375 Exhibit 4.1	04/23/2020
4.5	<a href="#">Form of Underwriters' Warrant Amendment Agreement.</a>		8-K	8011-34375 Exhibit 4.1	610/05/2020
4.6*	Form of Pre-Funded Warrant.				
4.7*	Form of Common Warrant.				
4.8*	Form of Placement Agent Warrant.				
5.1*	Opinion of Hogan Lovells US LLP.				

## Table of Contents

10.1+	<a href="#"><u>Patent and Know-How License Agreement, dated March 29, 2020, by and between Plus Therapeutics, Inc. and NanoTx, Corp.</u></a>	8-K	011-34375 Exhibit 10.1	3/30/2020
10.2+	<a href="#"><u>Patent &amp; Technology License Agreement, dated December 31, 2021, by and between Plus Therapeutics, Inc. and the University of Texas Health Science Center at San Antonio.</u></a>	10-K	011-34375 Exhibit 10.2	2/24/2022
10.3	<a href="#"><u>Equity Distribution Agreement, dated September 9, 2022, by and between Plus Therapeutics, Inc. and Canaccord Genuity LLC</u></a>	8-K	011-34375 Exhibit 1.1	09/09/2022
10.4	<a href="#"><u>Purchase Agreement, dated August 2, 2022, by and between Lincoln Park Capital Fund, LLC and Plus Therapeutics, Inc.</u></a>	8-K	011-34375 Exhibit 10.1	08/08/2022
10.5	<a href="#"><u>Registration Rights Agreement, dated August 2, 2022, by and between Plus Therapeutics, Inc. and Lincoln Park Capital Fund.</u></a>	8-K	001-34375 Exhibit 10.2	08/08/2022
10.6	<a href="#"><u>Loan and Security Agreement, dated May 29, 2015, by and among Plus Therapeutics, Inc. Oxford Finance, LLC, and lenders listed thereof.</u></a>	10-Q	001-34375 Exhibit 10.4	08/10/2015
10.7	<a href="#"><u>First Amendment to Loan and Security Agreement, dated September 20, 2017, by and among Plus Therapeutics, Inc., Oxford Finance, LLC and lenders listed thereof.</u></a>	S-1/A	333-219967 Exhibit 10.45	10/03/2017
10.8	<a href="#"><u>Second Amendment to Loan and Security Agreement, dated June 19, 2018, by and among Plus Therapeutics, Inc., Oxford Finance, LLC and lenders listed thereof.</u></a>	10-Q	001-34375 Exhibit 10.3	08/14/2018
10.9	<a href="#"><u>Third Amendment to Loan and Security Agreement, dated August 31, 2018, by and among Plus Therapeutics, Inc., Oxford Finance, LLC and lenders listed thereof.</u></a>	S-1	333-227485 Exhibit 10.51	09/21/2018
10.10	<a href="#"><u>Fourth Amendment to Loan and Security Agreement, dated December 31, 2018, by and among Plus Therapeutics, Inc., Oxford Finance, LLC. and lenders listed thereof.</u></a>	S-1	333-229485 Exhibit 10.52	02/01/2019
10.11	<a href="#"><u>Fifth Amendment to Loan and Security Agreement, dated January 31, 2019, by and among Plus Therapeutics, Inc., Oxford Finance, LLC and lenders listed thereof.</u></a>	10-K	001-34375 Exhibit 10.55	03/29/2019
10.12	<a href="#"><u>Sixth Amendment to Loan and Security Agreement, dated February 28, 2019, by and among Plus Therapeutics, Inc., Oxford Finance, LLC and lenders listed thereof.</u></a>	10-K	001-34375 Exhibit 10.56	03/29/2019
10.13	<a href="#"><u>Seventh Amendment to Loan and Security Agreement, dated April 24, 2019, by and among Plus Therapeutics, Inc., Oxford Finance, LLC and lenders listed thereof.</u></a>	10-Q	001-34375 Exhibit 10.3	05/14/2019

## Table of Contents

10.14	<a href="#"><u>Eight Amendment to Loan and Security Agreement, dated July 15, 2019, by and among Plus Therapeutics, Inc., Oxford Finance, LLC, and lenders listed thereof.</u></a>	10-Q	001-34375 Exhibit 10.2	08/15/2019
10.15+	<a href="#"><u>Ninth Amendment to Loan and Security Agreement, dated March 29, 2020, by and among Plus Therapeutics, Inc., Oxford Finance, LLC and lenders listed thereof.</u></a>	8-K	011-34375 Exhibit 10.2	3/30/2020
10.16	<a href="#"><u>Ten Amendment to Loan and Security Agreement, dated June 28, 2023, by and among Plus Therapeutics, Inc., Oxford Finance, LLC and lenders listed thereof.</u></a>	10-K	011-34375 Exhibit 10.16	3/5/2024
10.17#	<a href="#"><u>Amended and Restated Employment Agreement, dated March 11, 2020, by and between Marc Hedrick and Plus Therapeutics, Inc.</u></a>	10-Q	001-34375 Exhibit 10.6	5/16/2020
10.18#	<a href="#"><u>Amended and Restated Employment Agreement, dated March 11, 2020, by and between Andrew Sims and Plus Therapeutics, Inc.</u></a>	10-Q	001-34375 Exhibit 10.7	5/16/2020
10.19#	<a href="#"><u>Employment Agreement, dated December 8, 2021, by and between Plus Therapeutics, Inc. and Normal LaFrance</u></a>	8-K	001-34375 Exhibit 10.1	09/13/2021
10.20#	<a href="#"><u>2015 New Employee Incentive Plan.</u></a>	8-K	001-34375 Exhibit 10.1	01/05/2016
10.21#	<a href="#"><u>First Amendment to the Plus Therapeutics, Inc. 2015 New Employee Incentive Plan, dated January 26, 2017.</u></a>	10-K	001-34375 Exhibit 10.42	03/24/2017
10.22#	<a href="#"><u>Second Amendment to the Plus Therapeutics, Inc. 2015 New Employee Incentive Plan, dated February 6, 2020.</u></a>	10-K	001-34375 Exhibit 10.25	03/30/2020
10.23#	<a href="#"><u>Form of Notice of Grant of Stock Option under the 2015 New Employee Incentive Plan.</u></a>	S-8	333-210211 Exhibit 99.5	03/15/2016
10.24#	<a href="#"><u>Form of Stock Option Agreement under the 2015 New Employee Incentive Plan.</u></a>	S-8	333-210211 Exhibit 99.4	03/15/2016
10.25#	<a href="#"><u>Plus Therapeutics, Inc. 2020 Stock Incentive Plan, as amended and restated.</u></a>	8-K	001-34375 Exhibit 10.1	05/17/2021
10.26#	<a href="#"><u>Form of Notice of Grant and Stock Option Agreement under the 2020 Stock Incentive Plan.</u></a>	10-K	001-34375 Exhibit 10.26	02/24/2022
10.27+	<a href="#"><u>Master Services Agreement, dated January 24, 2021, by and between Piramal Pharma Solutions, Inc. and Plus Therapeutics, Inc.</u></a>	10-K	001-334275 Exhibit 10.24	02/22/2021
10.28#	<a href="#"><u>Form of Indemnification Agreement.</u></a>	8-K	001-34375 Exhibit 10.1	02/06/2020
10.29#	<a href="#"><u>Form of Agreement for Acceleration and/or Severance.</u></a>	10-K	001-34375 Exhibit 10.113	03/11/2016

## Table of Contents

10.30	<a href="#">Medidata Services Agreement and Statement of Work, dated November 5, 2021, by and between Medidata Solutions, Inc. and Plus Therapeutics, Inc.</a>	10-Q	001-34375 Exhibit 10.1	04/21/2022
10.31	<a href="#">Cancer Research Grant Contract, effective August 31, 2022, by and between the Cancer Prevention and Research Institute of Texas and Plus Therapeutics, Inc.</a>	8-K	001-34375 Exhibit 10.1	09/22/2022
10.32	<a href="#">Subscription and Investment Representation Agreement, dated March 3, 2023, by and between Plus Therapeutics, Inc. and the purchaser signatory thereto.</a>	8-K	001-34375 Exhibit 10.1	03/03/2023
10.33#	<a href="#">Plus Therapeutics, Inc. 2020 Stock Incentive Plan, as further amended and restated.</a>	8-K	001-34375 Exhibit 10.1	04/20/2023
10.34	<a href="#">Tenth Amendment to Loan and Security Agreement.</a>	10-Q	001-34375 Exhibit 10.2	08/14/2023
10.35*	Form of Securities Purchase Agreement.			
23.1	<a href="#">Consent of BDO USA, P.C.</a>	X		
23.2*	Consent of Hogan Lovells US LLP (included in Exhibit 5.1).			
24.1 †	<a href="#">Power of Attorney.</a>			
107	<a href="#">Fee Table.</a>	X		

- # Indicates management contract or compensatory plan or arrangement.  
+ Portions of this exhibit have been excluded pursuant to Item 601(b)(1)(iv).  
\* To be filed by amendment.  
† Previously filed.

**SIGNATURES**

Pursuant to the requirements of the Securities Act of 1933, the Registrant has duly caused this Amendment No. 1 to the Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Austin, State of Texas, on March 8, 2024.

**PLUS THERAPEUTICS, INC.**

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

Pursuant to the requirements of the Securities Act of 1933, this Amendment No. 1 to the 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, Chief Executive Officer and Director <i>(Principal Executive Officer)</i>	March 8, 2024
<u>/s/ Andrew Sims</u> Andrew Sims	Chief Financial Officer <i>(Principal Financial Officer and Principal Accounting Officer)</i>	March 8, 2024
<u>*</u> Richard J. Hawkins	Chairman of the Board	March 8, 2024
<u>*</u> Howard Clowes	Director	March 8, 2024
<u>*</u> An van Es-Johansson, MD	Director	March 8, 2024
<u>*</u> Robert Lenk, Ph.D.	Director	March 8, 2024
<u>*</u> Greg Petersen	Director	March 8, 2024

\* By: /s/ Mark H. Hedrick, MD  
Marc H. Hedrick, MD  
*Attorney-in-Fact*



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 March 5, 2024, relating to the 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, 2023. 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 such Prospectus.

/s/ BDO USA, P.C.

Austin, Texas  
March 8, 2024

## Calculation of Filing Fee Tables

**Form S-1**  
(Form Type)**Plus Therapeutics, Inc.**

(Exact Name of Registrant as Specified in its Charter)

Table 1: Newly Registered Securities

	Security Type	Security Class Title	Fee Calculation or Carry Forward Rule	Amount Registered	Proposed Maximum Offering Price Per Unit	Maximum Aggregate Offering Price <sup>(1)</sup>	Fee Rate	Amount of Registration Fee <sup>(2)</sup>
Fees Previously Paid	Equity	Common Stock, \$0.0001 par value per share <sup>(2)(3)</sup>	457(o)	—	—	\$8,000,000.00	\$0.00014760	\$1,180.80
	Other	Warrants to purchase Common Stock <sup>(4)</sup>	457(g)	—	—	—	—	\$0.00
Fees to Be Paid	Equity	Common Stock issuable upon exercise of Warrants to purchase Common Stock <sup>(2)</sup>	457(o)	—	—	\$8,000,000.00	\$0.00014760	\$1,180.80
	Other	Pre-Funded Warrants to purchase Common Stock <sup>(3)(4)</sup>	457(g)	—	—	—	—	\$0.00
	Equity	Common Stock issuable upon exercise of the Pre-Funded Warrants <sup>(2)(3)</sup>	457(o)	—	—	—	—	\$0.00
	Other	Placement Agent Warrants to purchase Common Stock <sup>(4)</sup>	457(g)	—	—	—	—	\$0.00
Fees to Be Paid	Equity	Common Stock issuable upon exercise of the Placement Agent Warrants <sup>(2)</sup>	457(o)				\$0.00014760	
	Total Offering Amounts					\$16,000,000.00	\$0.00014760	\$2,361.60
	Total Fees Previously Paid <sup>(5)</sup>							\$2,352.38
	Total Fee Offsets							—
	Net Fee Due							\$9.22

- (1) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(o) under the Securities Act of 1933, as amended (the "Securities Act").
- (2) Pursuant to Rule 416 under the Securities Act, the securities being registered hereunder include such indeterminate number of additional securities as may be issuable to prevent dilution resulting from stock splits, dividends or similar transactions.
- (3) The proposed maximum aggregate offering price of the common stock will be reduced on a dollar-for-dollar basis based on the offering price of any pre-funded warrants issued in the offering, and the proposed maximum aggregate offering price of the pre-funded warrants to be issued in the offering will be reduced on a dollar-for-dollar basis based on the offering price of any common stock issued in the offering. Accordingly, the proposed maximum aggregate offering price of the common stock and pre-funded warrants (including the common stock issuable upon exercise of the pre-funded warrants), if any, is \$8,000,000.00.
- (4) Pursuant to Rule 457(g) under the Securities Act, no separate registration fee is required for the warrants because the warrants are being registered in the same registration statement as the common stock issuable upon exercise of such warrants.

(5) The Registrant previously paid a filing fee of \$2,352.38 in connection with the initial filing of this Registration Statement on Form S-1 on November 22, 2023.