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

Form 8-K

Current Report

Pursuant to Section 13 or 15(d) of the
Securities Exchange Act of 1934

Date of Report (Date of earliest event reported)**: March 31, 2022**

PLUS THERAPEUTICS, INC.
(Exact name of registrant as specified in its charter)

Delaware	**001-34375**	**33-0827593**
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)

4200 Marathon Blvd., Suite 200, Austin, Texas 78756
(Address of principal executive offices, with zip code)

(737) 255-7194
(Registrant's telephone number, including area code)

N/A
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instructions A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001 per share	PSTV	The Nasdaq Capital Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).
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 13(a) of the Exchange Act. ☐

Item 1.01 Entry into a Material Definitive Agreement.

On March 31, 2022, Plus Therapeutics, Inc. (the "Company") and Medidata Solutions, Inc. ("Medidata") entered into a Statement of Work (the "SOW"), pursuant to which Medidata will build a Sythetic Control Arm® (SCA) platform that facilitates the use of historical clinical data to incorporate into the Company's Phase 2 clinical trial of Rhenium-186 NanoLiposome (^{186}RNL) in recurrent glioblastoma ("GBM"). The SOW is governed under the terms of a services agreement (the "Services Agreement"), dated November 5, 2021, between the Company and Medidata. Medidata's SCA is a type of external control that is formed by carefully selecting patients from Medidata's extensive repository of historical clinical trials to match the baseline demographic and disease characteristics of the patients treated with the new investigational product.

The SOW has a term of six (6) months. The Company will pay Medidata $1.45 million in managed services fees and a contingent managed services fee of $150,000 if the U.S. Food & Drug Administration approves a path forward for the Company to use the SCA in its clinical trial of ^{186}RNL for treatment of GBM. The SOW may only be terminated for a material breach by either party or if the clinical study's authorization or approval is withdrawn by a regulatory agency.

The foregoing description of the Services Agreement and SOW does not purport to be complete and is subject to, and qualified in its entirety by, the full text of the Services Agreement and SOW which will be filed by the Company with the Company's Quarterly Report on Form 10-Q for the quarter ending March 31, 2022.

Item 7.01 Other Events

On April 5, 2022, the Company issued a press release announcing the expanded partnership with Medidata. A copy of the press release is attached hereto as Exhibit 99.1 and is incorporated herein by reference.

The information in this Item 7.01, including Exhibit 99.1, is being furnished and not filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended and will not be incorporated by reference into any filing under the Securities Act of 1933, as amended, unless specifically identified therein as being incorporated therein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit Number	Description
99.1	Press Release Announcing Expanded Relationship with Medidata, dated April 5, 2022.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: April 5, 2022

PLUS THERAPEUTICS, INC.

By: /s/ Marc H. Hedrick, M.D.

Marc H. Hedrick, M.D.

President and Chief Executive Officer

Exhibit 99.1

Plus Therapeutics and Medidata Announce Expanded Clinical Trial Partnership

Companies collaborate to design innovative registrational trial of ^{186}RNL for recurrent glioblastoma

Proprietary Synthetic Control Arm® solution intended to enhance enrollment and reduce costs

AUSTIN, Texas, April 5, 2022 – Plus Therapeutics, Inc. (Nasdaq: PSTV) (the "Company"), a clinical-stage pharmaceutical company developing innovative, targeted radiotherapeutics for rare and difficult-to-treat cancers, today announced that it has expanded its partnership with Medidata, a Dassault Systèmes company.

The goal of the expanded partnership is to speed enrollment, improve patient access to an innovative therapy and reduce clinical trial costs in Plus Therapeutics' planned forthcoming Phase 2 registrational trial of Rhenium-186 NanoLiposome (^{186}RNL) in recurrent glioblastoma (GBM). The partnership will utilize Medidata's Synthetic Control Arm® (SCA) platform that facilitates the use of historical clinical trial (HCT) data in a manner that historically has been favorably received by the U.S. Food and Drug Administration. The expanded partnership follows a successful preliminary assessment stage intended to determine project feasibility and probability of success.

"Synthetic control arms reduce the time and cost associated with complex clinical trials in rare diseases such as glioblastoma," said Norman LaFrance, M.D., Chief Medical Officer and SVP of Plus Therapeutics. "Plus has been quite impressed with Medidata's team, capabilities and platform in the recently completed feasibility phase. Furthermore, the benefit is passed down to patients and their families, allowing for fewer patients to be exposed to placebos or existing standard-of-care treatments that might not be effective for them, offering them greater access to potentially life-extending therapies."

Medidata will provide the Company with a SCA based on a historical pool of anonymized HCT data to incorporate into Plus Therapeutics' planned Phase 2 trial of ^{186}RNL in recurrent GBM. SCAs are especially advantageous in indications such as recurrent GBM where the standard-of-care control treatment is considered undesirable by many patients and physicians.

About the Synthetic Control Arm®

Medidata's Synthetic Control Arm (SCA) – a type of external control – is formed by carefully selecting patients from Medidata's extensive repository of historical clinical trials to match the baseline demographic and disease characteristics of the patients treated with the new investigational product. Case studies have shown that SCAs can effectively mimic a classic randomized control and, therefore, can be used to accurately interpret the treatment effects of an investigational product.

SCAs can help enhance the scientific validity of single-arm trials and, in certain indications, enhance randomized clinical trials to expose fewer prospective patients to control and/or ineffective or existing standard-of-care treatments that might not provide a benefit to the patient. This is done while still

providing highly valid scientific evidence. These factors can influence a patient's willingness to participate in a trial where there is a very poor prognosis and perceived inadequate standard of care.

About Plus Therapeutics

Plus Therapeutics, Inc. is a clinical-stage pharmaceutical company focused on the development, manufacture, and commercialization of complex and innovative treatments for patients battling cancer and other life-threatening diseases.

Our proprietary nanotechnology platform is currently centered around the enhanced delivery of a variety of drugs using novel liposomal encapsulation technology. Liposomal encapsulation has been extensively explored and undergone significant technical and commercial advances since it was first developed. Our platform is designed to facilitate new delivery approaches and/or formulations of safe and effective, injectable drugs, potentially enhancing the safety, efficacy and convenience for patients and healthcare providers. More information may be found at PlusTherapeutics.com and ReSPECT-Trials.com.

Cautionary Statement Regarding Forward-Looking Statements

This press release contains statements that may be deemed "forward-looking statements" within the meaning of U.S. securities laws. All statements in this press release other than statements of historical fact are forward-looking statements. These forward-looking statements may be identified by future verbs, as well as terms such as "designed to," "will," "can," "potential," "focus," "preparing," "next steps," "possibly," and similar expressions or the negatives thereof. Such statements are based upon certain assumptions and assessments made by 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 the following: the potential promise of 186RNL including the ability of 186RNL to safely and effectively deliver radiation directly to the tumor at high doses; expectations as to the Company's future performance including the next steps in developing the Company's current assets; the Company's clinical trials including the use of a synthetic control armpossible negative effects of 186RNL; the continued evaluation of 186RNL including through evaluations via a seventh patient cohort; and the intended functions of the Company's platform and expected benefits from such functions.

The forward-looking statements included in this press release are subject to a number of risks and uncertainties that may cause actual results to differ materially from those discussed in such forward-looking statements. These risks and uncertainties include, but are not limited to: the Company's actual results may differ, including materially, from those anticipated in these forward-looking statements as a result of various factors, including, but not limited to, the following: the early stage of the Company's product candidates and therapies, the results of the Company's research and development activities, including uncertainties relating to the clinical trials of its product candidates and therapies; the Company's liquidity and capital resources and its ability to raise additional cash, the outcome of the Company's partnering/licensing efforts, risks associated with laws or regulatory requirements applicable to it, market conditions, product performance, litigation or potential litigation, and competition within the regenerative medicine field, among others; and additional risks described under the heading "Risk Factors" in the Company's Securities and Exchange Commission filings, including in the Company's

annual and quarterly reports. There may be events in the future that the Company is unable to predict, or over which it has no control, and its business, financial condition, results of operations and prospects may change in the future. The Company assumes no responsibility to update or revise any forward-looking statements to reflect events, trends or circumstances after the date they are made unless the Company has an obligation under U.S. federal securities laws to do so.

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