Plus Therapeutics Completes Dosing in Cohort 4 of ReSPECT-LM Phase 1 Clinical Trial of Rhenium (^{186}Re) Obisbemeda in Leptomeningeal Metastases

October 10, 2023

Cohort 4 of the ReSPECT-LM Phase 1 dose escalation trial is the first of 4 planned cohorts in Part B; the Company anticipates moving into Cohort 5 following standard safety review

Updates on the ReSPECT-LM trial and on the ReSPECT-GBM trials in recurrent glioblastoma are planned for November 15-19 at the Society for Neuro-Oncology Annual Meeting

AUSTIN, Texas, Oct. 10, 2023 (GLOBE NEWSWIRE) -- Plus Therapeutics, Inc. (Nasdaq: PSTV) (the "Company"), a clinical-stage pharmaceutical company developing targeted radiotherapeutics with advanced platform technologies for central nervous system cancers, today announced it has completed dosing in Cohort 4 of the ReSPECT-LM Phase 1/2a dose escalation clinical trial of rhenium (^{186}Re) obisbemeda for the treatment of leptomeningeal metastases (LM) from solid tumors. In addition, the Company has completed the transfer of proprietary materials, protocols, and equipment from Biocept under the terms of the recently announced expanded agreement for CNSide, a cerebrospinal fluid (CSF)-based tumor cell capture and enumeration assay being utilized in the ReSPECT-LM clinical trial.

"The speed at which we are enrolling in the ReSPECT-LM trial reflects multiple factors, including the increasing number of patients diagnosed with LM, the lack of good therapeutic options and growing enthusiasm for the trial," said Marc H. Hedrick M.D., President and Chief Executive Officer of Plus Therapeutics. "Furthermore, significant updates on both the ReSPECT-LM and ReSPECT-GBM studies are planned for November 15-19, 2023 at the Society for Neuro-Oncology (SNO) Annual Meeting."

Phase 1, Part A of the ReSPECT-LM trial (Cohorts 1-3) is complete and demonstrated an average 53% reduction in CNSide tumor cell counts at Day 28 post-treatment in 10 patients receiving a single administration of rhenium (^{186}Re) obisbemeda. The FDA has approved continued dose escalation and expansion into Part B (Cohorts 4-7). Completion of dosing in Cohort 4 was the fastest enrollment of all the Cohorts to date. There have been no observed dose limiting toxicities with radiation doses of up to 44.10 millicuries. The Company plans to initiate dosing in Cohort 5 this quarter, pending Data Safety Monitoring Board (DSMB) approval. After the update at the SNO meeting in November, the Company anticipates additional data releases in 2024.

The CNSide assay has potential as: an LM diagnostic assay, a surrogate endpoint in clinical trials for CNS cancers such as LM, and as a disease monitoring biomarker assay in the management of patients undergoing radiotherapy for LM. The acquired materials and protocols from Biocept help ensure Plus' access to the CNSide assay in the ongoing ReSPECT-LM Phase 1 clinical trial with rhenium (^{186}Re) obisbemeda. Plus Therapeutics retains its option, solely at the Company's discretion, to acquire an exclusive field of use license on the CNSide assay in return for a $1.0 million payment, if exercised prior to January 1, 2025.

The FDA has granted Fast Track designation to rhenium (^{186}Re) obisbemeda for the treatment of LM, and the ReSPECT-LM Phase 1 program continues to be funded in part by a 3-year $17.6 million grant from the Cancer Prevention & Research Institute of Texas (CPRIT). Patients interested in learning more about the ReSPECT-LM trial can visit ClinicalTrials.gov (NCT05034497).

About Leptomeningeal Metastases (LM)
LM is a rare complication of cancer in which the primary cancer spreads to the cerebrospinal fluid (CSF) and leptomeninges surrounding the brain and spinal cord. All malignancies originating from solid tumors, primary brain tumors, or hematological malignancies have this LM complication potential with breast cancer as the most common cancer linked to LM, with 3-5% of breast cancer patients developing LM. Additionally, lung cancer, GI cancers and melanoma can also spread to the CSF and result in LM. LM occurs in approximately 5% of people with cancer and is usually terminal with 1-year and 2-year survival of just 7% and 3%, respectively. The incidence of LM is on the rise, partly because cancer patients are living longer and partly because many standard chemotherapies cannot reach sufficient concentrations in the spinal fluid to kill the tumor cells, yet there are no FDA-approved therapies specifically for LM patients, who often succumb to this complication within weeks to several months, if untreated.

About Rhenium (^{186}Re) obisbemeda
Rhenium (^{186}Re) obisbemeda is a novel injectable radiotherapy specifically formulated to deliver highly targeted high dose radiation in CNS tumors in a safe, effective and convenient manner to optimize patient outcomes. Rhenium (^{186}Re) obisbemeda has the potential to reduce risks and improve outcomes for CNS cancer patients, versus currently approved therapies, with a more targeted and potent radiation dose. Rhenium-186 is an ideal radioisotope for CNS therapeutic applications due to its short half-life, beta energy for destroying cancerous tissue and gamma energy for live imaging. Rhenium (^{186}Re) obisbemeda is being evaluated for the treatment of recurrent glioblastoma and leptomeningeal metastases in the ReSPECT-GBM and ReSPECT-LM clinical trials. ReSPECT-GBM is supported by an award from the National Cancer Institute (NCI), part of the U.S. National Institutes of Health (NIH), and ReSPECT-LM is funded by a three-year $17.6M grant by the Cancer Prevention & Research Institute of Texas (CPRIT).

About CNSide
CNSide is an assay based on proprietary quantitative tumor cell capture method paired with advanced digital imaging and molecular markers used to detect, characterize, and quantify tumor cells in CSF of patients with a variety of solid organ carcinomas and suspected LM, particularly breast and lung cancer which are leading causes of LM. *CNSide* provides a robust quantitative method to evaluate tumor status and response to treatment compared to conventional CSF cytology or radiologic monitoring.

In March 2023, Biocept initiated enrollment in the FORESEE trial with *CNSide*. The FORESEE trial is a two-part, multicenter, prospective clinical trial expected to enroll up to 40 patients with breast or non-small cell lung cancer who have suspicious or confirmed LM. The goal of the FORESEE trial is to evaluate the performance of *CNSide* in monitoring LM's response to treatment and to assess the impact of *CNSide* on treatment decisions made by

physicians. The feasibility phase of the study is expected to complete in the first half of 2024, which will be followed by a validation phase that is estimated to include between 40 and 100 subjects.

About Plus Therapeutics

Plus Therapeutics, Inc. is a clinical-stage pharmaceutical company developing targeted radiotherapeutics for difficult-to-treat cancers of the central nervous system with the potential to enhance clinical outcomes for patients. Combining image-guided local beta radiation and targeted drug delivery approaches, the Company is advancing a pipeline of product candidates with lead programs in recurrent glioblastoma (GBM) and leptomeningeal metastases (LM). The Company has built a robust supply chain through strategic partnerships that enable the development, manufacturing and future potential commercialization of its products. Plus Therapeutics is led by an experienced and dedicated leadership team and has operations in key cancer clinical development hubs including Austin and San Antonio, Texas. For more information, visit https://plustherapeutics.com/.

[1]The CNSide assay is not an FDA cleared or approved assay. It is a Biocept lab developed test and its performance characteristics were determined in Biocept's CLIA-certified, CAP-accredited laboratory.

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 ^{186}Re including the ability of ^{186}Re 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 statements regarding the timing and characteristics of the ReSPECT-GBM and ReSPECT-LM clinical trials; possible negative effects of ^{186}Re; the continued evaluation of ^{186}Re including through evaluations in additional patient cohorts; 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 cancer diagnostics and therapeutics 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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