Plus Therapeutics Announces Validation & Clinical Implementation of CSF-01 Leptomeningeal Cancer Cell Diagnostic

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Plus' CSF-01 cancer cell enumeration test is a sensitive and specific diagnostic test for the presence of adenocarcinoma and melanoma cancer cells in the leptomeninges

CSF-01 testing is used as an exploratory endpoint in the ReSPECT-LM trials

Controlled clinical trial data evaluating the utility of CSF-01 in clinical decision-making is anticipated to be released in Q2/Q3 2024

AUSTIN, Texas, March 25, 2024 (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 (CNS) cancers, today announced it has successfully completed key validation testing and implementation of its tumor cell enumeration assay, known as CSF-01, to be used initially as an exploratory endpoint in its ReSPECT-LM clinical trials.

"Plus' CSF-01 tumor cell enumeration assay is a highly specific and sensitive diagnostic test that is promising for both establishing the diagnosis of leptomeningeal metastases (LM) and following the disease course over time," said Dr. Priya Kumthekar, Associate Professor, Feinberg School of Medicine, Northwestern University**.** "Current diagnostic methods lack the sensitivity and specificity to reliably inform clinical decision making, and the field is excited about the use of CSF-01 in the ReSPECT-LM trials as an exploratory endpoint and hopefully soon, for use in all patients in which LM is in the differential diagnosis."

Plus' CSF-01 cancer cell enumeration test is an exploratory endpoint in the ReSPECT-LM Phase 1 trial that has shown promise in the trial's early cohorts. In Phase 1/Part A of the ReSPECT-LM trial presented at the 2023 SNO/ASCO Meeting in San Francisco, Plus showed an average 53% reduction in CSF tumor cells 28 days after a single intrathecal administration of rhenium (^{186}Re) obisbemeda in patients with LM.

"In mid-2023, the Company licensed CSF-01, as well as a broader CSF diagnostic testing portfolio due to high conviction that routine implementation will substantially improve diagnosis and clinical management of LM," said Marc H. Hedrick, M.D., President & CEO of Plus Therapeutics. "Our initial objective was to make the test available for our ReSPECT-LM trial patients, which is now complete. Now, we are evaluating the FORSEE clinical trial data, which we anticipate reporting in the second or third quarter of 2024."

On December 12, 2023, Plus announced its partnership with K2bio (Houston, Texas) to implement Plus' CSF-01 diagnostic for LM cancers in the ReSPECT-LM trials. While validated for use in Plus' clinical development programs, full Clinical Laboratory Improvement Amendments (CLIA) certification is not anticipated until 2025. The ReSPECT-LM trial, including support for CSF-01 testing, is currently receiving grant funding from the Cancer Prevention and Research Institute of Texas (CPRIT).

The FORSEE trial was performed by the original developer and licensor of CSF-01 and is a multi-center, prospective clinical trial enrolling patients with breast or non-small cell lung cancer (NSCLC) who have suspicious or confirmed LM. If the FORSEE data is positive, we intend to work toward increasing commercial reimbursement for the CLIA-certified test and explore partnerships to maximize diagnostic utilization for the broader CNS cancer space.

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 a 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 directly 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 off-target 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 real-time 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 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 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/.

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, including statements regarding clinical trials, expected operations and upcoming developments. 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 "potential," "anticipating," "planning" 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 rhenium (^{186}Re) obisbemeda including the ability of rhenium (^{186}Re) obisbemeda 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, ReSPECT-LM and ReSPECT-PBC and increase of ten o, clinical trials; possible negative effects of rhenium (^{186}Re) obisbemeda; the continued evaluation of rhenium (^{186}Re) obisbemeda 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 could differ materially from those expressed or implied by these forward-looking statements because of risks, uncertainties, and other factors that include, but are 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, ability to develop and protect proprietary intellectual property or obtain licenses to intellectual property developed by others on commercially reasonable and competitive terms, and material security *breach* or cybersecurity attack affecting the Company's operations or property. This list of risks, uncertainties, and other factors is not complete. Plus Therapeutics discusses some of these matters more fully, as well as certain risk factors that could affect Plus Therapeutics' business, financial condition, results of operations, and prospects, in its reports filed with the SEC, including Plus Therapeutics' annual report on Form 10-K for the fiscal year ended December 31, 2023, quarterly reports on Form 10-Q, and current reports on Form 8-K. These filings are available for review through the SEC's website at www.sec.gov. Any or all forward-looking statements Plus Therapeutics makes may turn out to be wrong and can be affected by inaccurate assumptions Plus Therapeutics might make or by known or unknown risks, uncertainties, and other factors, including those identified in this press release. Accordingly, you should not place undue reliance on the forward-looking statements made in this press release, which speak only as of its date. 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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