Plus Therapeutics Provides Updates on ReSPECT™ Clinical Trials at the 27th Annual Scientific Meeting and Education Day of the Society for Neuro-Oncology

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ReSPECT-GBM clinical trial of rhenium (^{186}Re) obisbemeda in recurrent glioblastoma continues to demonstrate safety and overall survival correlates with radiation dose to tumor

ReSPECT-GBM Phase 2 trial enrollment has begun

Update on ReSPECT-LM clinical trial and first-in-child Phase 1/2a pediatric brain cancer trial for ependymoma and high-grade glioma

AUSTIN, Texas, Nov. 19, 2022 (GLOBE NEWSWIRE) -- Plus Therapeutics, Inc. (Nasdaq: PSTV) (the "Company"), a clinical-stage pharmaceutical company developing innovative, targeted radiotherapeutics for rare and difficult-to-treat cancers, presented data from two ongoing clinical trials evaluating the Company's lead investigational targeted radiotherapeutic, rhenium (^{186}Re) obisbemeda, in recurrent glioblastoma (GBM), leptomeningeal metastases (LM), as well as clinical trial plans for pediatric brain cancer at the 27th Annual Scientific Meeting and Education Day of the Society for Neuro-Oncology (SNO).

"Targeted radiotherapy using rhenium (^{186}Re) obisbemeda in patients with GBM and LM has, thus far, been shown to be both feasible and safe across a range of dosages and a variety of delivery parameters. Furthermore, it is unusual to see such a tight correlation between overall survival and absorbed dose at this point of clinical development," said Andrew J. Brenner, M.D., Ph.D., Professor of Medicine, Neurology, and Neurosurgery at The University of Texas Health Science Center at San Antonio and principal investigator of the ReSPECT-GBM and ReSPECT-LM clinical trials. "This data strongly supports continued clinical development for several very difficult to treat CNS indications."

The oral presentation titled, **Report of the ReSPECT-GBM Phase 1/2a Dose Escalation Trial of Rhenium-186 NanoLiposome (^{186}RNL) in Recurrent Glioma via Convection Enhanced Delivery (CED) & Planned Phase 2b Trial** [RADT-20], included the following key findings:

- In 24 patients with recurrent glioblastoma, a single dose of rhenium (^{186}Re) obisbemeda was administered in the dose escalation phase, (range: 1.0 mCi/0.66 mL to 31.2 mCi/12.3 mL), achieving up to 740 Gray (Gy) of absorbed radiation dose to the tumor.
- Between one to four intracranial CED catheters have been placed in each patient and there have been no dose limiting toxicities and a good safety profile has been observed.
- A statistically significant improvement in overall survival correlated with both the average absorbed dose of radiation to the tumor and the percent volume of tumor treated, specifically:
    - A 100 Gy increase in the absorbed dose correlated with a 35.7% decrease in the risk of death (p=0.003, Cox methods hazard ratios = 0.643)
    - A 1% increase in tumor volume treated is associated with a 4.5% decrease in the risk of death (p=0.002, Cox methods hazard ratios = 0.955)
- A recommended Phase 2 dose of 22.3 mCi in 8.8 mL is being studied for tumor volumes of 20 mL or less and is expected to enroll up to an additional 31 patients.
- Continued dose escalation will be performed to assess the potential to treat tumors larger than 20 mL.

The Company's second oral presentation titled, **Preclinical Data and Initial Clinical Experience in the Phase 1/2a Dose Escalation Trial of Rhenium-186 Nanoliposome (^{186}RNL) in Leptomeningeal Metastases [LM]: the ReSPECT-LM Trial** [CTNI-02], highlighted data from the first two cohorts which demonstrates the potential of rhenium (^{186}Re) obisbemeda to treat LM:

- As single rhenium (^{186}Re) obisbemeda dose administered through an intraventricular catheter (Ommaya reservoir) at 6.6 mCi in 5.0 mL in Cohort 1 achieved absorbed doses of 18.7 to 29.0 Gy to the ventricles and cranial subarachnoid space, which was well tolerated with no treatment-related adverse events of greater than grade 1.
- All four patients treated to date in Cohorts 1 and 2 were observed to have prompt and complete rhenium (^{186}Re) obisbemeda distribution throughout the cerebrospinal fluid (CSF) subarachnoid space that was durable to 28 days.
- All patients showed a decreased CSF tumor cell count by microfluidic chamber assay after treatment, ranging from 46% to 92%.

In November 2022, Plus Therapeutics, in collaboration with Lurie Children's Hospital investigators, anticipates filing an Investigational New Drug (IND) application for a first-in-child Phase 1/2a clinical trial to determine the maximum tolerated dose, safety, tolerability and early efficacy of rhenium (^{186}Re) obisbemeda in supratentorial recurrent or progressive pediatric ependymoma and high-grade glioma (HGG) in up to 24 patients initially. These

plans were presented in a poster titled, **A two-part, Phase 1 study of Rhenium-186 NanoLiposome (^{186}RNL) delivered by convection enhanced delivery (CED) for recurrent or progressive childhood ependymoma and high-grade glioma (HGG)** [CTNI-19].

“Ependymoma and HGG are difficult-to-treat pediatric brain tumors that are frequently aggressive, and in recurrent settings, can carry extremely poor prognoses for these children,” said Norman LaFrance, M.D., Chief Medical Officer and Senior Vice President at Plus Therapeutics. “The standard of care for pediatric brain cancer is insufficient given the current limitations surrounding traditional external beam radiation therapy. However, we believe rhenium (^{186}Re) obisbemeda has potential to overcome these obstacles and more effectively manage this devastating disease, given our initial data seen in adults with recurrent glioblastoma. We look forward to working with the FDA to advance the pediatric study.”

Copies of the presentations will be available under the Presentations tab of the Investors section of the Company's website at the time of the presentations at https://ir.plustherapeutics.com.

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 ^{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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