Plus Therapeutics Presents Positive Phase 1 Data from ReSPECT-GBM Clinical Trial at the European Society for Medical Oncology Congress 2022

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Phase 1 data indicates that direct administration of ^{186}RNL targeted radiotherapeutic is safe in patients with recurrent glioblastoma

Statistically significant overall survival benefit observed with ^{186}RNL radiation doses over 100 Gray

NIH-funded trial moving to Phase 2 to explore expanded dosing parameters, treat larger tumor sizes, and gather additional safety and efficacy data, that will support a future registrational trial

AUSTIN, Texas, Sept. 12, 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, today announced Phase 1 data from the ReSPECT-GBM Phase 1/2a dose escalation clinical trial evaluating the Company's lead investigational targeted radiotherapeutic, Rhenium-186 NanoLiposome (^{186}RNL), in recurrent glioblastoma (GBM) in an oral presentation at the European Society for Medical Oncology (ESMO) Congress 2022, being held September 9-13, 2022 in Paris, France.

"Radiation is lethal to cancer cells and rhenium-186 is an ideal radioisotope for the treatment of glioblastoma. Furthermore, the unique drug formulation allows the radiation to stay in the brain for days, if not weeks," 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 clinical trial. "In the ReSPECT-GBM Phase 1 trial, we achieved up to 20 times the amount of radiation compared to external beam radiation therapy, and we observed a statistically significant improvement in survival in those patients receiving a therapeutic dose of radiation compared to those that did not."

The oral presentation titled, **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** [2770], reviews data from the Phase 1 ReSPECT-GBM trial which evaluated 23 adult patients with recurrent GBM across 8 cohorts of increasing dose and treated over a seven-year period.

Key findings include:

- No dose-limiting toxicities (DLT) have been observed and the procedure is very well tolerated with a strong safety profile. Minimal systemic radiation has been observed and the majority of adverse events have been mild or moderate and considered causally unrelated to the procedure.
- Improved median overall survival (OS) rates correlated with the absorbed tumor radiation dose. When patients were stratified based on receipt of either a therapeutic or a subtherapeutic absorbed dose of radiation to the tumor, a statistically significant improvement in survival was observed. Specifically, patients receiving a therapeutic absorbed radiation dose (>100 Gray) had a median OS of 22.9 (95% CI of 8.8-42.3) months compared to those receiving a subtherapeutic absorbed radiation dose (<100 Gray) whose median OS was 5.6 months (95% CI of 1.6-9.4). Currently, three patients remain alive, all in the therapeutic group.
- Feasibility to deliver up to at least 20 times more radiation to the tumor than the standard of care, external beam radiation therapy (EBRT). A maximum of 32.2 mCi in 12.3 mL of volume has been delivered in and near the tumors, and a maximum average absorbed dose of radiation of 740 Gray has been successfully administered in a single procedure.
- Average absorbed radiation dose to the tumor increased in latter dosing cohorts with greater administered doses of Re-186 β-particle radiation, larger drug convection enhanced delivery (CED) infusate volumes, more catheters used (up to 4 versus 1), and higher convection flow rates. In cohorts 5 and later, 82% of patients received a therapeutic radiation dose of >100Gray.
- Single-photon emission computerized tomography and (SPECT)/CT scanning were used during treatment to compute tumor coverage and dosimetry. Post treatment imaging analyses, including MRI, relative cerebral blood volume (rCBV) analysis and treatment response assessment maps (TRAMs) correlated with a positive tumor response and confirmed the presence of pseudoprogression in patients with positive tumor responses.
- ReSPECT-GBM will proceed to an NIH and U.S. Food and Drug Administration (FDA) approved Phase 2 trial in the U.S. at the current non-DLT ^{186}RNL dose and will expand exploring higher radiation doses in larger volumes to treat larger tumors. Additionally, two or more ^{186}RNL 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.

"The Phase 1 data offer important and objective insight and data into ^{186}RNL's potential to safely prolong patient survival and suggests that there is an overall survival benefit when a ^{186}RNL dose of more than 100 Gray is achieved," said Norman LaFrance, M.D., Chief Medical Officer and Senior Vice President at Plus Therapeutics. "The planned Phase 2 study using cGMP ^{186}RNL will leverage a higher dose and volume that could potentially show a

greater survival rate in patients with recurrent GBM."

Based upon feedback from a Type C meeting with the FDA, the Company plans to initiate the ReSPECT-GBM Phase 2 trial in the second half of 2022, funded principally by the NIH. The Company intends to begin the ReSPECT-GBM Phase 2 trial utilizing cGMP ^{186}RNL drug, which will be available in the second half of 2022. In this study, researchers plan to administer the recommended non-DLT dose of 22.3 mCi (total 186RNL activity) at a concentration of 2.5 mCi/mL in 8.8 mL total volume to patients with a tumor size of less than or equal to 20 cm^3 as a starting point. Furthermore, the Company plans to evaluate further doses, including both increased dosing and multiple doses, and collect additional safety and efficacy data for the planned future registrational trial.

A copy of the presentation will be available under the Presentations tab of the Investors section of the Company's website at the time of presentation 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}RNL including the ability of ^{186}RNL 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}RNL; the continued evaluation of ^{186}RNL 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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