



Plus Therapeutics Announces First Patient Dosed in Phase 1/2a Dose Escalation Trial of ¹⁸⁶RNL Radiotherapeutic for Leptomeningeal Metastases

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ReSPECT-LM trial to evaluate safety/tolerability and identify MTD/MFD in three cohorts

Rhenium-186 NanoLiposome (¹⁸⁶RNL) now in two active U.S. clinical trials for CNS cancers

AUSTIN, Texas, March 22, 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 that the first patient has been dosed in the ReSPECT-LM Phase 1/2a dose escalation clinical trial of Rhenium-186 NanoLiposome (¹⁸⁶RNL) for the treatment of patients with leptomeningeal metastases (LM).

The investigational drug, ¹⁸⁶RNL, is a proprietary nanoscale compound with a unique chelated radioisotope that is administered locally as a single dose via a conventional Ommaya reservoir. Rhenium-186 is a dual energy emitter (beta and gamma) with a short average path length for high precision, low dose rate that is safer for normal tissues, and high radiation density that overwhelms innate DNA repair mechanisms. The dual energy emission allows real time evaluation and monitoring of the ¹⁸⁶RNL administration.

The disease target, solid tumor-originating LM, is a deadly and increasingly common central nervous system (CNS) complication potentially from all solid cancer, with breast cancer, lung cancer, gastrointestinal cancer and melanoma being the most common primary sources of LM, with 110,000 cases diagnosed annually in the U.S. LM affects the membranes (meninges) surrounding the brain and spinal cord. There are currently no meaningfully effective Food and Drug Administration-approved treatments.

"The rationale for use of ¹⁸⁶RNL in LM patients is scientifically quite attractive, and in clinical practice was very straightforward to administer to our first patient," said Michael Youssef, M.D., Assistant Professor of Neuro-Oncology at University of Texas Southwestern and site Principal Investigator. "Quality of life and survival rates are poor among patients diagnosed with LM from solid tumors. With no standard of care, this represents a true unmet medical need in neuro-oncology."

"LM affects about 10 times the number of patients as glioblastoma but carries a substantially worse prognosis," said Norman LaFrance, M.D., Chief Medical Officer and SVP of Plus Therapeutics. "Initiating treatment in LM patients with ¹⁸⁶RNL marks an important milestone for Plus Therapeutics and potentially for the LM patient population."

The ReSPECT-LM trial ([NCT05034497](#)) is a multicenter, sequential cohort, open-label, single dose, dose escalation Phase 1/2a study using a modified Fibonacci 3+3 study design. It will evaluate the maximum tolerated dose (MTD), maximum feasible dose (MFD), safety and efficacy of a single administration of ¹⁸⁶RNL via intraventricular catheter for LM following standard surgical, radiation and/or chemotherapy treatment. The primary endpoints of the study are the incidence and severity of adverse events/serious adverse events and dose limiting toxicities. Secondary endpoints include overall response rate, duration of response, progression free survival and overall survival.

The ReSPECT-LM Phase 1/2a clinical trial follows [preclinical studies](#) in which tolerance to doses of ¹⁸⁶RNL as high as 1,075 Gy was shown in animal models with LM with no observed significant toxicity. Treatment led to marked reduction in tumor burden in two animal models of LM.

The Company recently [announced](#) the FDA granted Fast Track designation to ¹⁸⁶RNL for the treatment of LM. Fast Track designation confers several benefits to the drug development program including 1) more frequent meetings with and written communication from FDA, 2) eligibility for Accelerated Approval and Priority Review, if relevant criteria are met, and 3) Rolling Review, which allows a drug company to submit completed sections of its New Drug Application (NDA) for review by FDA, rather than wait until every section of the NDA is completed before the entire application can be reviewed.

About Leptomeningeal Metastases (LM)

LM is a rare complication of cancer in which the disease spreads to the membranes (meninges) surrounding the brain and spinal cord. LM occurs in approximately 5% of people with cancer and is usually terminal with one-year and two-year survival of just 7% and 3% respectively. LM can originate from solid tumors, primary brain tumors, or hematological malignancies.

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 statements regarding the timing and characteristics of the ReSPECT-LM or the ReSPECT-PBC trials; possible 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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