Plus Therapeutics Announces FDA Clearance of its Investigational New Drug Application using REYOBIQ™ for the Treatment of Childhood Brain Cancer

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Phase 1/2a clinical trial currently supported by a $3.0 million grant from the U.S. Department of Defense

Trial will enroll children with high grade glioma and ependymoma

HOUSTON, June 25, 2025 (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 that the U.S. Food and Drug Administration (FDA) has cleared its Investigational New Drug (IND) application (No. 168178) for REYOBIQ™ (Rhenium Re186 Obisbemeda) for the treatment of pediatric patients with supratentorial recurrent, refractory, or progressive high-grade glioma (HGG) and ependymoma. The trial will be referred to as the ReSPECT-PBC trial and is funded by a $3.0M research grant from the U.S. Department of Defense.

"We are very excited for the opportunity to study the novel radiotherapeutic, REYOBIQ, in difficult-to-treat pediatric brain tumors. Surgery and external beam radiation have been the mainstays of treatment for pediatric high-grade glioma and, sadly, outcomes have not improved for many decades. We believe this novel therapy that may allow higher doses of radiation while limiting the exposure to normal developing brain and delivering this agent via convection enhanced delivery (CED) directly into the tumor has the potential to make a big difference in our patients' lives and improve outcomes," said Dr. Ashley S. Plant, M.D., Principal Investigator for the trial, attending physician in Hematology, Oncology, Neuro-oncology, and Stem Cell Transplantation at Ann & Robert H. Lurie Children's Hospital of Chicago, A.M. Khokhar Research Scholar and Associate Professor of Pediatrics at Feinberg School of Medicine Northwestern University. "I am extremely passionate about bringing this therapy into the pediatric space and hopeful about the benefits to my patients."

Phase 1/2a Trial Design Highlights:

The Phase 1/2a trial is a two-part, single-arm, prospective study aimed at determining the maximum tolerated dose (MTD), safety, and tolerability of REYOBIQ in pediatric patients aged 6 to 21 years (with consideration for patients up to 25 years on a case-by-case basis).

Key elements of the trial design include:

- Phase 1a/b (Dose Escalation): This phase will enroll an estimated 24 patients using a modified 3+3 dose escalation scheme to establish the MTD and recommended Phase 2 dose (RP2D). Safety assessment and alignment with the FDA will occur at defined intervals.
- Phase 2a: This phase will enroll approximately 32 patients (12 with ependymoma and 20 with HGG) at the RP2D to assess efficacy.

Pediatric HGG including ependymoma are rare (approximately 3.3 cases per 100,000 persons) but aggressive brain tumors with limited treatment options and poor prognosis, particularly in recurrent settings. Standard treatments, including surgical resection and external beam radiation therapy, often fail to prevent recurrence, with 5-year survival rates as low as 22% for HGG, depending on tumor grade and resection extent. REYOBIQ's targeted delivery via CED bypasses the blood-brain barrier, offering a novel approach to potentially improve outcomes for these patients.

"This pediatric FDA clearance builds on our successful track record in the safe administration and promising efficacy signals observed in adult patients with more common central nervous cancers," said Marc Hedrick, M.D., Plus Therapeutics President and Chief Executive Officer. "We expect REYOBIQ will offer much needed hope to children with aggressive and difficult-to-treat brain cancers and their families."

REYOBIQ is a novel radiotherapeutic designed to deliver high doses of beta radiation directly to brain tumors while minimizing damage to surrounding healthy tissue. The ReSPECT-PBC (pediatric brain cancer) trial builds on promising preclinical data and clinical results from the Company's adult recurrent glioblastoma trial (ReSPECT-GBM). As recently published in *Nature Communications*, ReSPECT-GBM demonstrated favorable safety and clinical response with a doubling of overall survival for those patients receiving a therapeutic dose of radiation defined as > 100 Gy.

For more information, please contact @plustherapeutics.com or visit www.clinicaltrials.gov (identifier to be assigned upon registration).

About REYOBIQ™ (rhenium Re^{186} obisbemeda)

REYOBIQ™ (rhenium Re^{186} obisbemeda) is a novel injectable radiotherapy specifically formulated to deliver direct targeted high dose radiation in CNS tumors in a safe, effective, and convenient manner to optimize patient outcomes. REYOBIQ™ 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. REYOBIQ™ 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). The Company's clinical trial for pediatric brain cancer is supported by a $3 million grant from the U.S. Department of Defense's Peer Reviewed Cancer Research Program.

About Plus Therapeutics

Headquartered in Houston, Texas, 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. Combining image-guided local beta radiation and targeted drug delivery approaches, the Company is advancing a pipeline of product candidates with lead programs in leptomeningeal metastases (LM) and recurrent glioblastoma (GBM) and pediatric brain cancer (PBC). The Company has built a supply chain through strategic partnerships that

enable the development, manufacturing, and future potential commercialization of its products. For more information, visit https://plustherapeutics.com/.

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 trial design, clinical outcomes, product candidates, 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 “expect” “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.

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 Company’s ability to maintain the listing of its common stock on Nasdaq; risks related to a halt in trading or delisting of the Company’s common stock on Nasdaq; 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; 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; challenges associated with radiotherapeutic manufacturing; production and distribution capabilities necessary to support the Company’s clinical trials and any commercial level product demand; 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, 2024, 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 incorrect 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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