Preliminary Clinical data in the Phase 1/2a Dose Escalation Trial of 186RNL (Rhenium-186 nanoliposome) (186Re) Obisbemeda in Leptomeningeal Metastases (LM): the ReSPECT-LM Trial

***W. Phillips*[1]**, *A. Bao*[2], *N. LaFrance*[3], *M. Hedrick*[3], *M. Moore*[3], *T. Patel*[4], *J. Floyd*[1], *M. Youssef*[4], *J. Michalek*[1], *A. Brenner*[1];*

[1]The University of Texas Health Science Center at San Antonio, San Antonio, TX, UNITED STATES OF AMERICA, [2]Case Western Reserve University, San Antonio, TX, UNITED STATES OF AMERICA, [3]Plus Therapeutics, Inc, Austin, TX, UNITED STATES OF AMERICA, [4]UT Southwestern Medical Center, Dallas, TX, UNITED STATES OF AMERICA.

Aim/Introduction: Leptomeningeal metastases (LM) are a devastating clinical complication where the primary cancer spreads to the leptomeninges. Treatment options for LM are limited, and survival is dismal. Rhenium (186Re) obisbemeda (186RNL) is a BMEDA-chelated 186Re encapsulated in nanoliposomes β-emitter with a ~2 mm path length, allowing directly targeted radiation therapy delivery with limited exposure to surrounding tissue. We present preliminary clinical data for the first 9 patients from our ReSPECT-LM trial (NCT05034497). **Materials and Methods:** ReSPECT-LM is a multi-center, sequential cohort, open-label, dose-escalation, phase 1/2a clinical trial evaluating the safety, tolerability, and activity of a single dose of 186RNL given by a direct CNS intraventricular [Ommaya Reservoir] route in LM adult patients. Primary objectives are: maximum tolerated dose/ maximum feasible dose in up to 21 LM patients in 7 cohorts using a modified 3x3 Fibonacci design, 3 cohorts have been enrolled beginning at 6.6 mCi with administered dose doubling at each successive cohort to 26.4mCi administered in 5 mL through a Ommaya reservoir. Whole body planar and SPECT/CT imaging were obtained up to 7 days following treatment for dosimetry, distribution and CSF tumor cells/ml using microfluidic chamber assay were assessed up to 56 days. Patients were followed for safety, progression, and survival. **Results:** A total of 9 LM patients [3 each in Cohorts 1-3} have been treated. Patients had primary diagnoses of small cell carcinoma, metastatic breast cancer (both triple negative), and lung adenocarcinoma. 186RNL showed prompt, complete distribution throughout the CSF with durable retention in the subarachnoid space and leptomeninges through protocol defined observation on Day 7 and achieved absorbed doses ranging from 18.7 to ~200 Gray (Gy) to the ventricles and cranial subarachnoid spaces. All patients experienced a decreased CSF cell count ranging from 46% to 92%. Patient treatment started in March of 2022, eight patients remain alive [1 patient has died due to primary tumor progression. No patients had treatment related adverse events (AEs) greater than Grade 1, and the most common AE was headache. **Conclusion:** Preliminary, interim results of this ongoing phase 1 trial showed that a single treatment with 186RNL delivered by an intraventricular catheter (Ommaya reservoir) in 9 adult patients is well tolerated, without dose limiting toxicity and with decreased CSF tumor cell counts durable through at least 30 days. Enrollment and dose escalation is continuing, and repeated dosing will be explored.