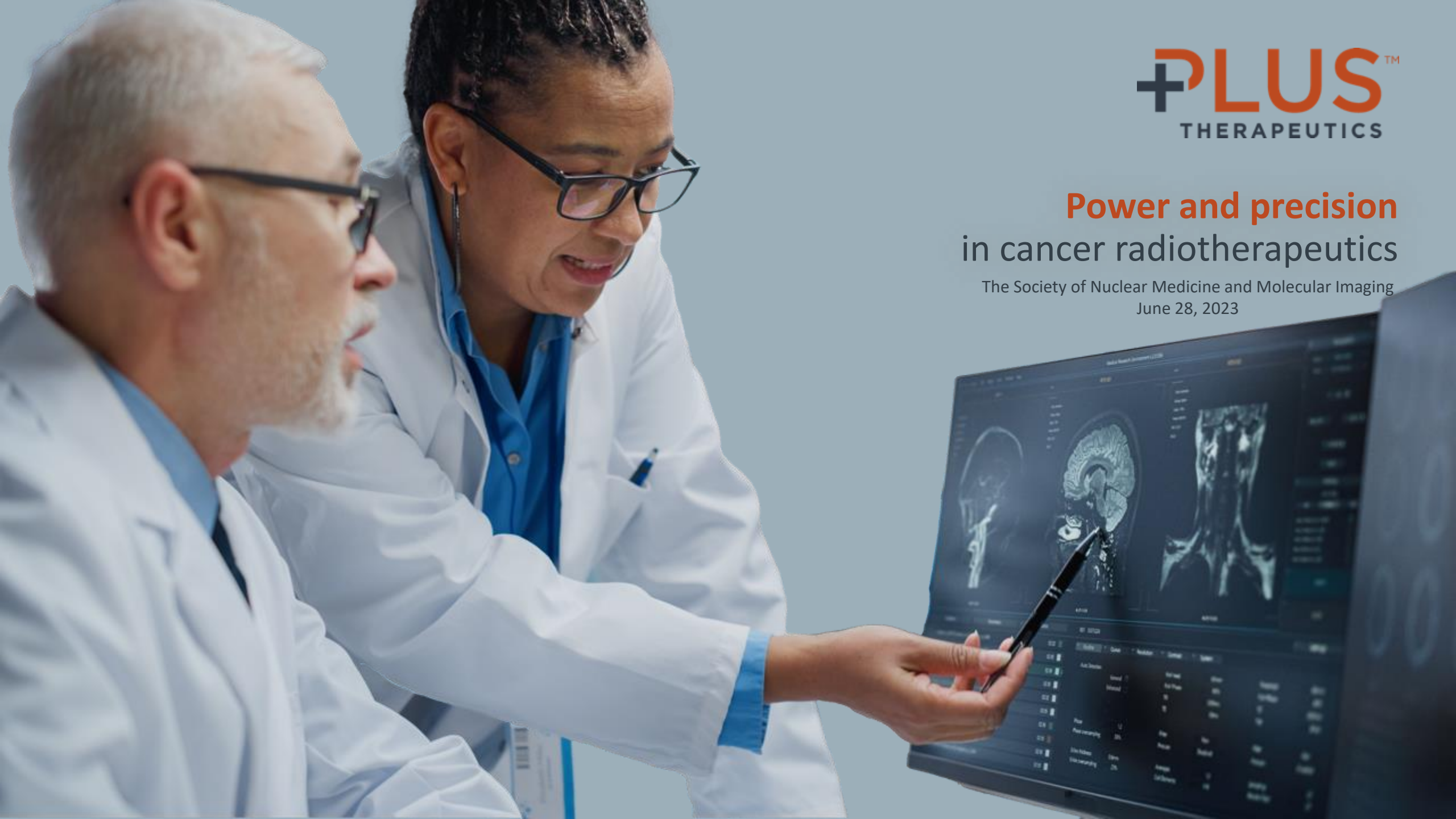


PLUS™ THERAPEUTICS

Power and precision
in cancer radiotherapeutics

The Society of Nuclear Medicine and Molecular Imaging
June 28, 2023

Forward Looking Statement

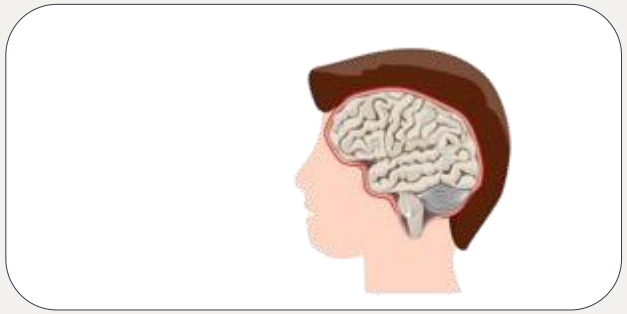
This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Any statement in this document that is not a historical fact is a “forward-looking statements” within the meaning of Section 27A of the Securities Act & Section 21E of the Securities Exchange Act & are usually identified by the use of words such as “anticipates,” “believes,” “estimates,” “expects,” “intends,” “may,” “plans,” “projects,” “seeks,” “should,” “will,” & variations of such words or similar expressions. We intend these forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act & Section 21E of the Securities Exchange Act of 1934, as amended, & are making this statement for purposes of complying with those safe harbor provisions. These forward-looking statements reflect our current views about our plans, intentions, expectations, strategies & prospects, which are based on the information currently available to us & on assumptions we have made. Although we believe that our plans, intentions, expectations, strategies & prospects as reflected in or suggested by those forward-looking statements are reasonable, we can give no assurance that the plans, intentions, expectations or strategies will be attained or achieved. Furthermore, actual results may differ materially from those described in the forward-looking statements & will be affected by a variety of risks & factors that are beyond our control.

Risks & uncertainties for Plus include, but are not limited to: the early stage of Plus’s product candidates and therapies, the results of Plus’s research and development activities, including uncertainties relating to the clinical trials of its product candidates and therapies; Plus’s liquidity and capital resources and its ability to raise additional cash, the outcome of Plus’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 Plus’s Securities and Exchange Commission filings, including in Plus’s annual and quarterly reports. There may be events in the future that Plus 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. Plus assumes no responsibility to update or revise any forward-looking statements to reflect events, trends or circumstances after the date they are made unless Plus has an obligation under U.S. federal securities laws to do so.

PLUS Direct Targeted Drug Delivery Strategies for CNS Cancers

Overcomes the primary ‘barrier’ to CNS drug development

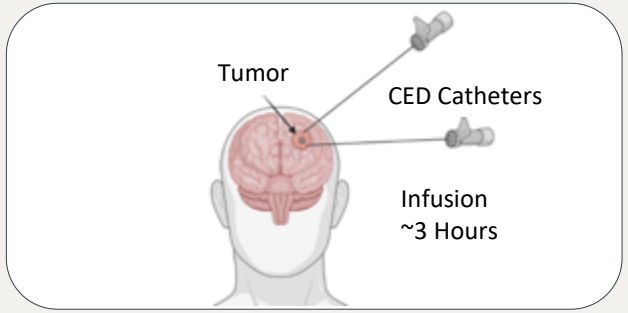
Blood-Brain-Barrier (BBB)



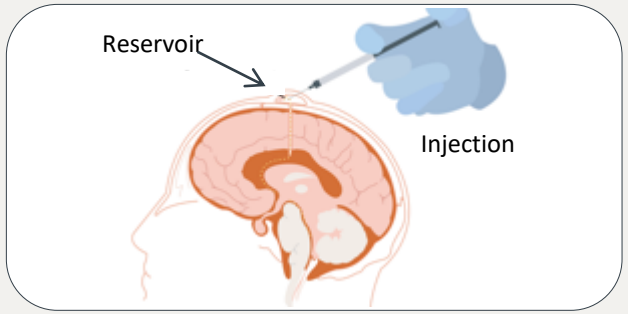
CNS Drug Delivery Limitations

+ Network of closely spaced cells for CNS protection
+ Prevents >98% of systemically delivered drugs from reaching a therapeutic concentration in the brain

Brain Parenchyma



Cerebrospinal Fluid



Convection-Enhanced Delivery (CED)

+ FDA-approved and utilized for 20+ years
+ Bypasses BBB
+ ‘Biological fracking’: Controlled pressure and flow rate provides optimal drug delivery to region of interest
+ Standard technology found in any hospital with neurosurgery

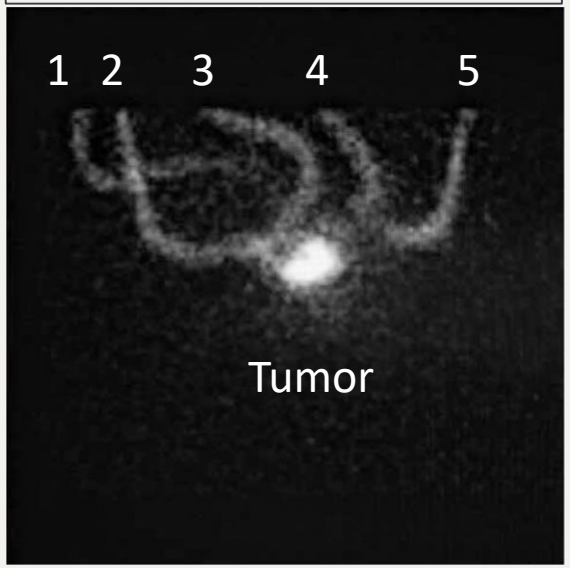
Ommaya Reservoir

+ FDA-approved and utilized for 60+ years
+ Bypasses BBB
+ Small reservoir is placed under the scalp and allows drug to be directly delivered to the ventricle
+ Allows multi-drug dosing and CSF sampling
+ Commonly placed in LM patients

Visualization and Monitoring of CED in Real-Time via γ emission

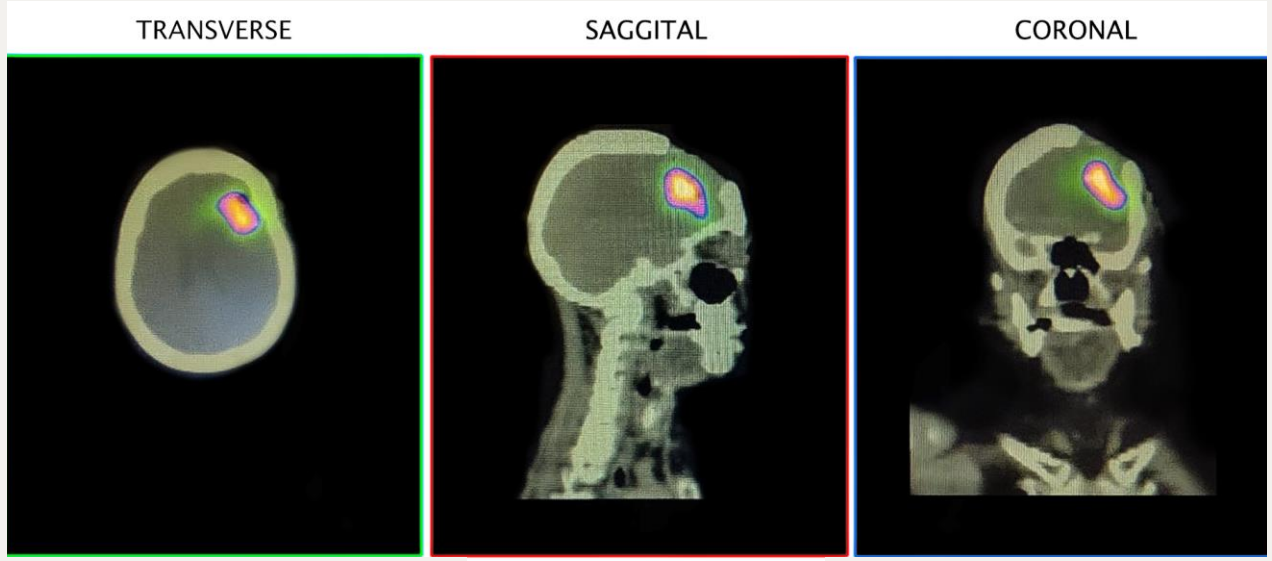
ReSPECT Trial Patient, use of up to 5 catheters feasible

5 Catheter CED



Planar SPECT Image During Infusion

SPECT/CT Image at 20% Total Infusion



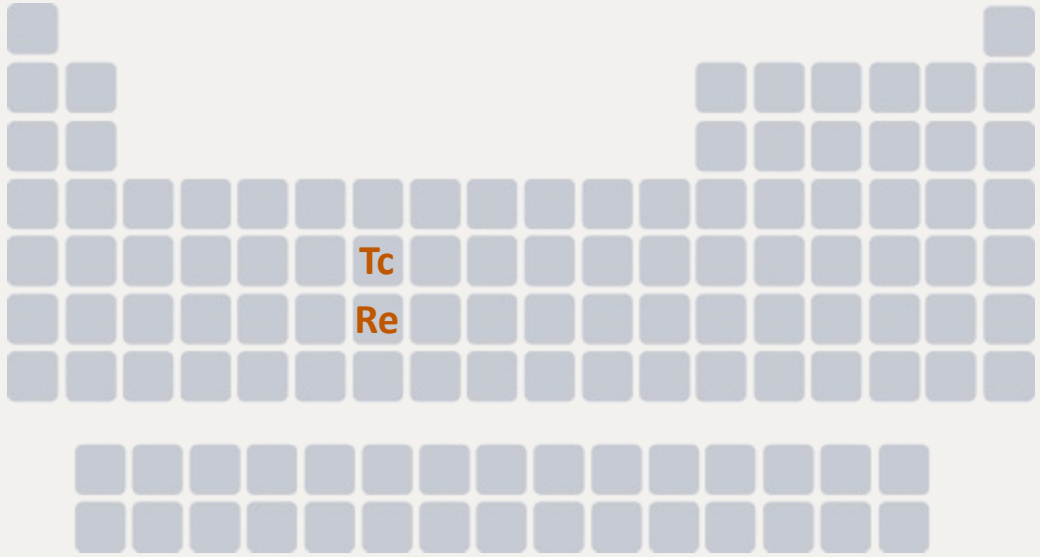
20% INFUSION SPECT/CT

PLUS Uses Isotopic Rhenium for CNS Indications

Ideal radioisotope for CNS tumors

+ Two clinically relevant isotopes, Rhenium-186 & Rhenium-188
+ 'Goldilocks' energy profile between Yttrium-90 & Lutetium-177
+ Dual energy: β is tumoricidal & γ for imaging
+ Rhenium/BMEDA chemistry is ideal for nanoliposome loading
+ Lacks affinity for bone & thyroid
+ Rapid clearance
+ High radiation density & optimal half-life
+ Mature, redundant supply chain

	Rhenium-186	Rhenium-188
Average path length	~ 2 mm	~ 4 mm
Radiation half life	3.8 days	17 hours
Manufacture	Reactor	Generator



+ **Technetium (Tc) is adjacent in the periodic table to Rhenium (Re) and have similar properties**
+ **Tc is used in 40 million diagnostic procedures per year (80% of all nuclear medicine procedures globally)**

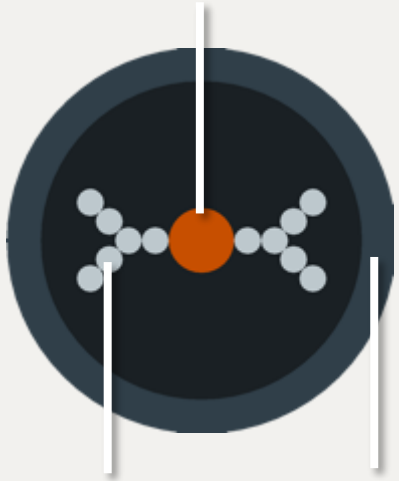
PLUS' Lead Drug Rhenium Re^{186} Obisbemeda Prolongs Radiation in the Brain & CSF

Complementary technologies drive efficacy & safety profile

Rhenium Re^{186} Obisbemeda

Rhenium-186 Radionuclide

Emits tumor destroying radiation over short distances while sparing healthy tissue



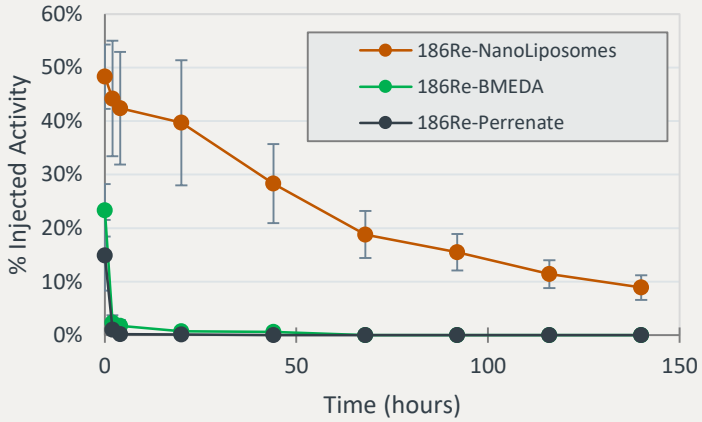
BMEDA Small Molecule

Chelates to Rhenium & is loaded into a NanoLiposome where it is irreversibly trapped

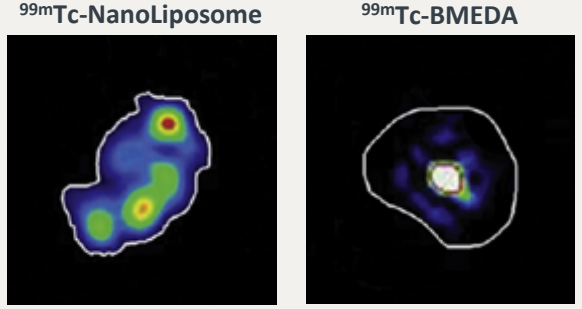
100 nm NanoLiposome

Carries BMEDA-Rhenium to target tumor & improves retention

Tumor Retention



Improved Drug Distribution Coverage

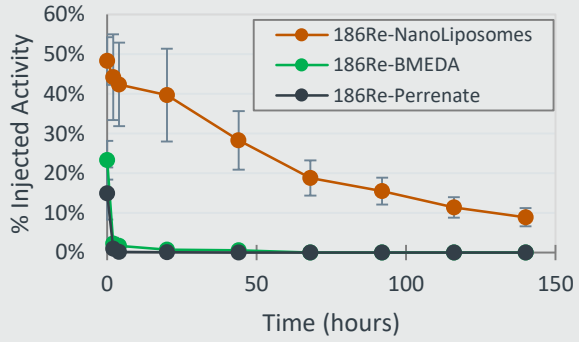


Sources: Phillips, W. et al. *Advanced Drug Delivery Reviews,* 2014

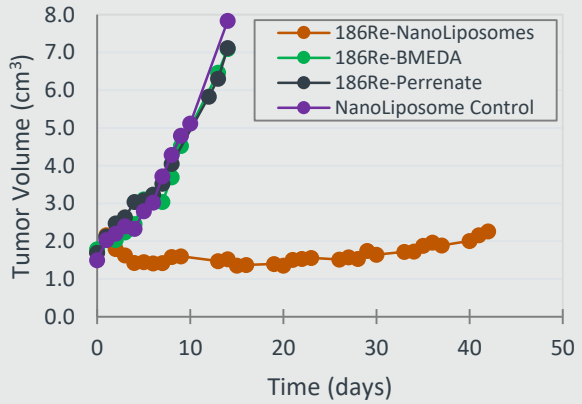
Preclinical Evidence for Rhenium Re^{186} Obisbemeda Use in CNS Cancers

Nanoliposome Enhances Tumor Dispersion & Response

Tumor Retention

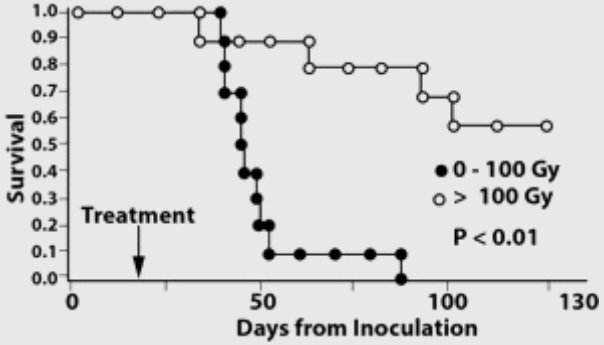


Tumor Response

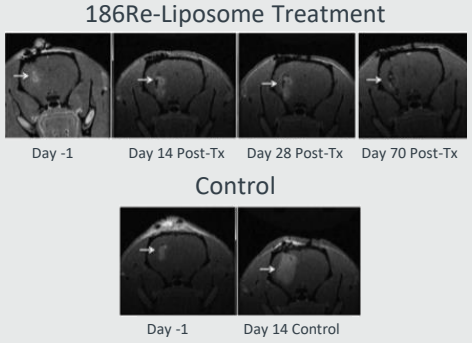


Glioblastoma Intracranial Xenograft Model

Clear Separation in Rat Survival at a Radiation Dose of 100 Gray

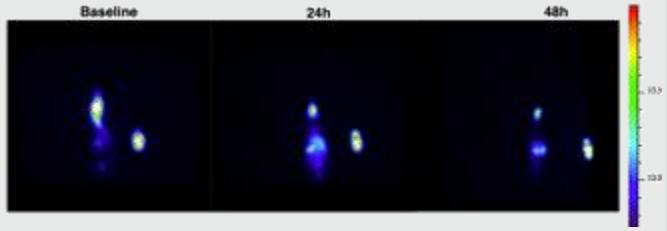


^{186}Re Treated Tumors Progressively Disappear Over Time

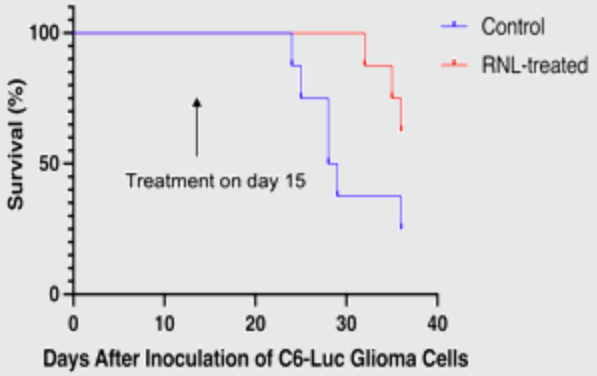


Leptomeningeal Metastases Wistar Rat Model

Radioactivity Visualized at 48 Hours; Mean Absorbed Radiation Dose of 1,094 Gy



Statistically Significant Difference in Overall Survival with ^{186}RNL-Treated Animals Outliving the Controls

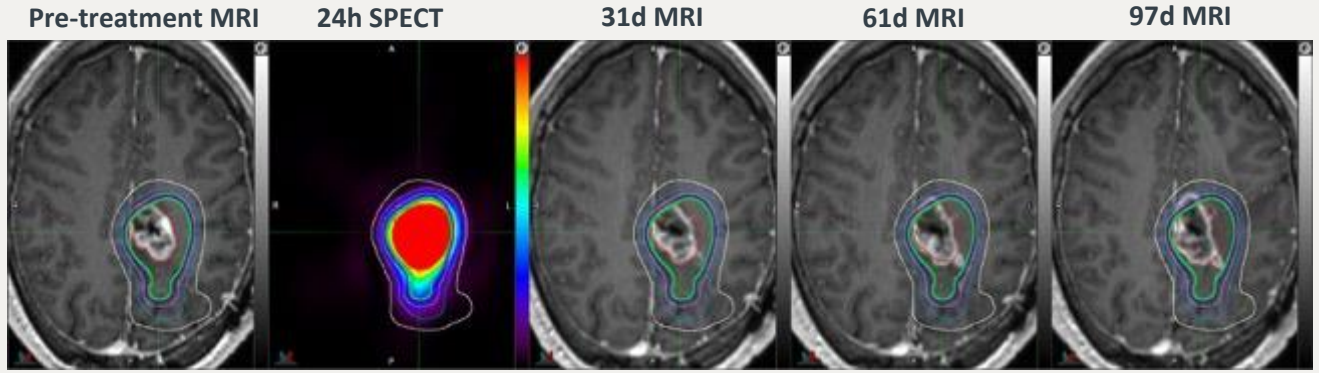


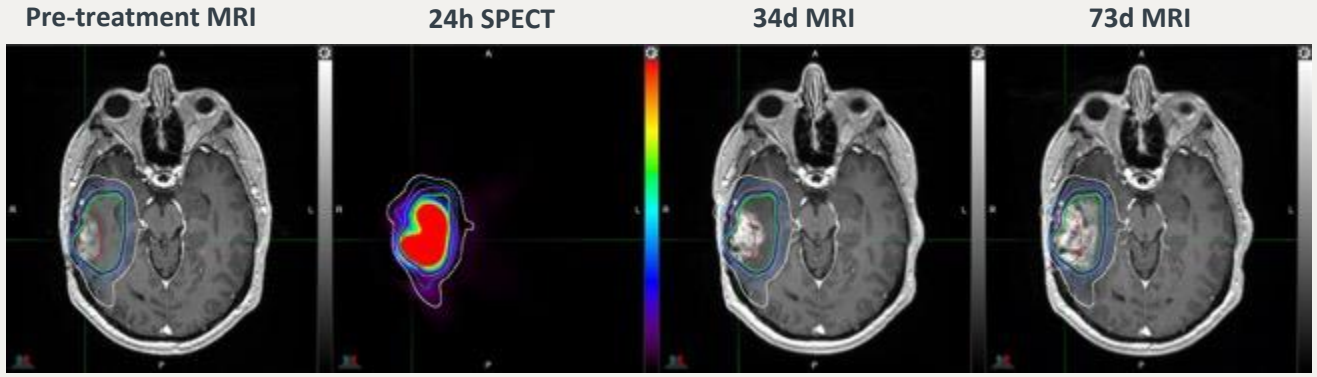
Sources: Phillips, W. et al. *Advanced Drug Delivery Reviews,* 2014; Phillips, W. et al. *Neuro-Oncology*, 2012; Balinda, H. et al. *SNO Brain Metastases Meeting,* 2021

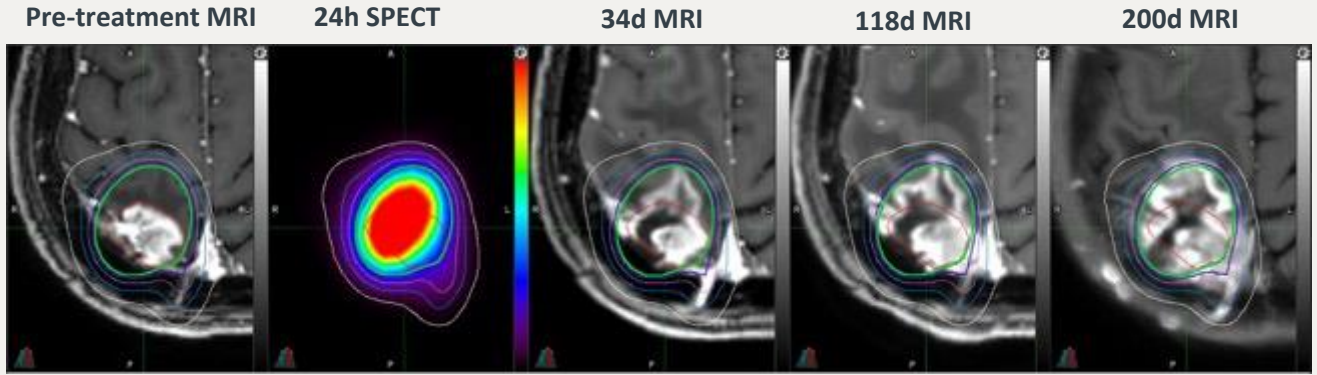
ReSPECT-GBM Trial for Recurrent Glioblastoma

3 case studies from ReSPECT-GBM Phase 1 Trial

(OS between 750 & 1200 days, 2 alive)







ReSPECT-GBM Trial for Recurrent Glioblastoma

Phase 1 Safety Profile (n=27 patients)

Serious Adverse Event Possibly Related to Study Drug	Grade 1 Mild	Grade 2 Moderate	Grade 3 Severe	Total
Decreased platelet count	0	1	0	**1**
Cerebral edema	0	0	1	**1**
Lymphopenia	0	0	1	**1**

+ No catheterization complications
+ The majority of adverse events are Grade 1 or 2 in severity & unrelated to study drug
+ Minimal systemic radiation exposure observed

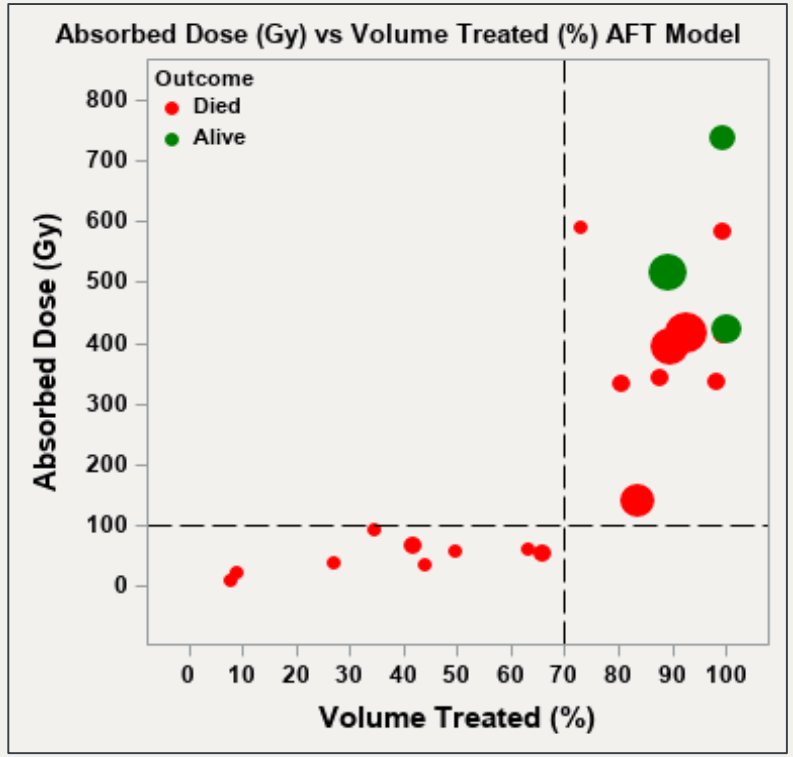
ReSPECT-GBM Trial for Recurrent Glioblastoma

Phase 1 efficacy data through RP2D determination (n=21 patients)

Dose Escalation Trial

- Very poor prognostic group of recurrent GBM patients
- 6 dose escalation cohorts, range:
  - Volume: 0.66 to 8.8 mL
  - Dose: 1.0 to 22.3 mCi
- RP2D: 22.3 mCi/8.8 mL
- No treatment failures
- 1-4 catheters used
- Increased tumor coverage & dose at higher dose cohorts
- Publication pending

Patient Response: Dose vs. Tumor Coverage



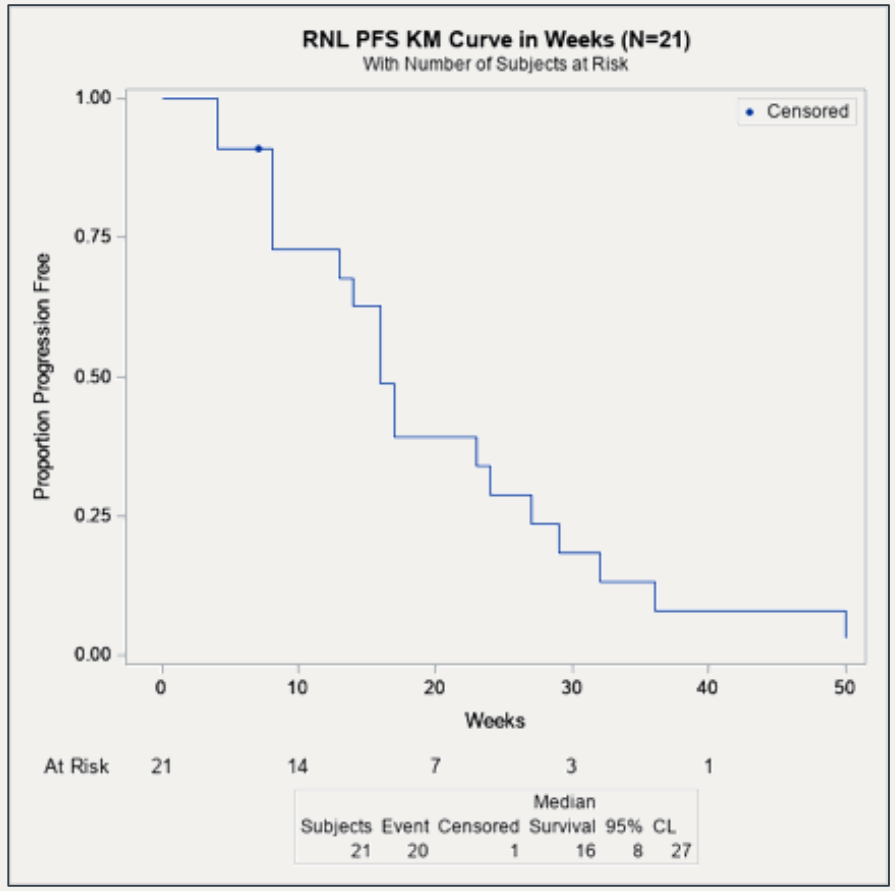
100 Gy threshold based on preclinical observations

Accelerated Failure Time (AFT) Model: Parametric model complements the Cox Proportional Hazards Model

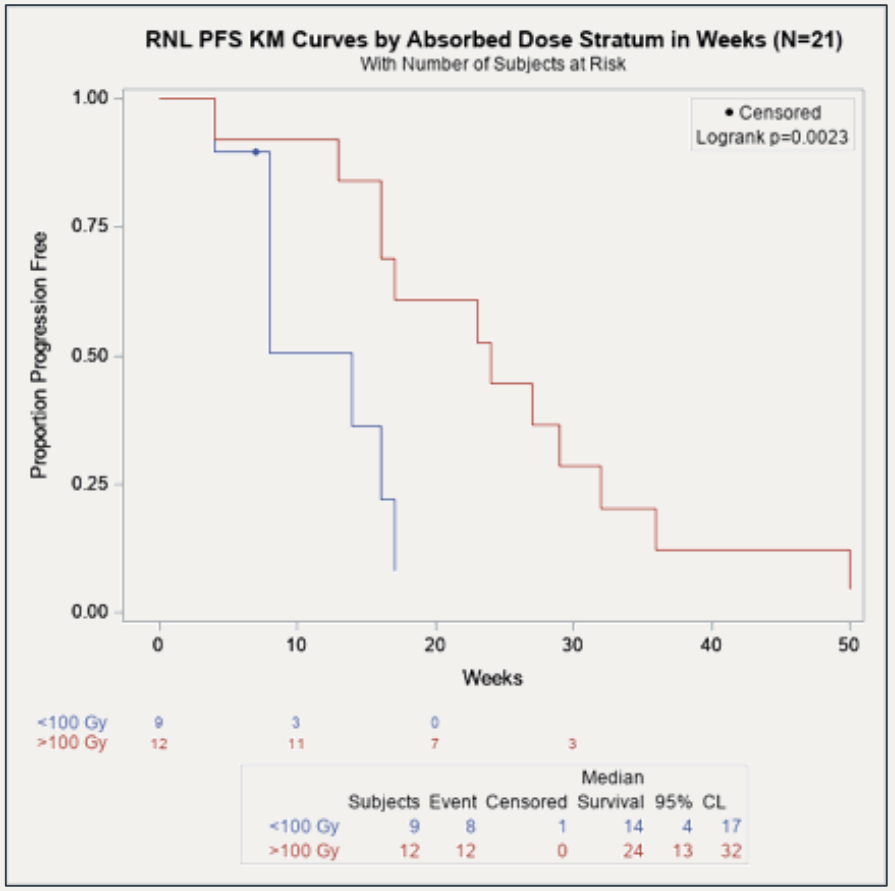
ReSPECT-GBM Trial for Recurrent Glioblastoma

Phase 1 efficacy data through RP2D determination (n=21 patients)

Progression Free Survival



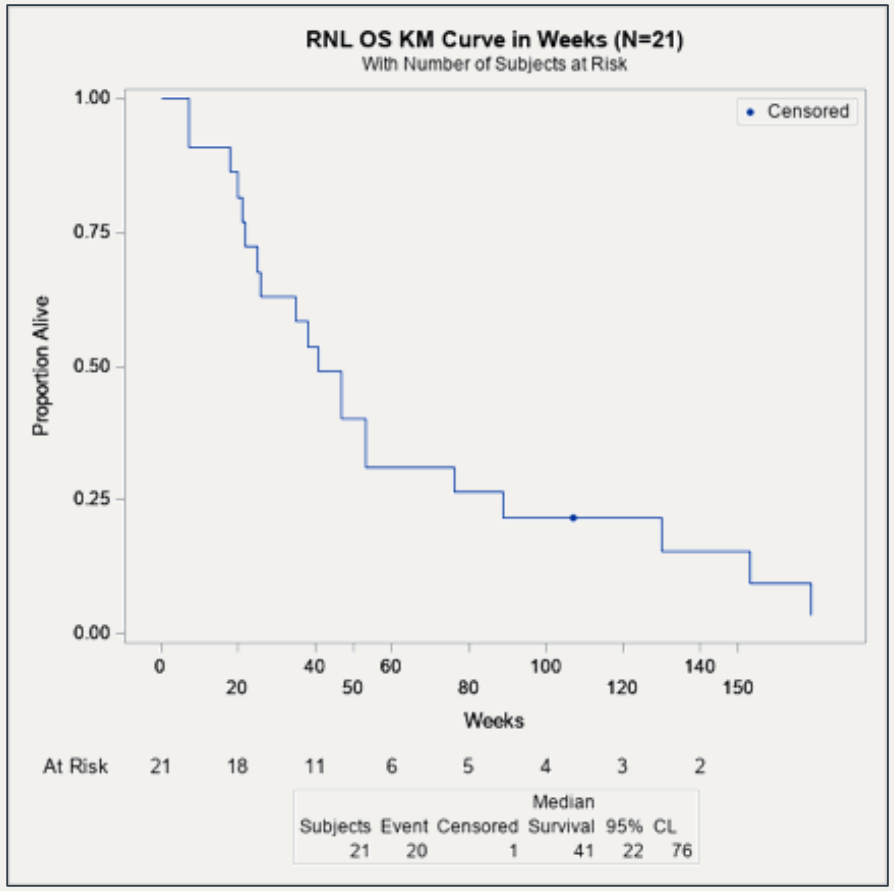
Progression Free Survival



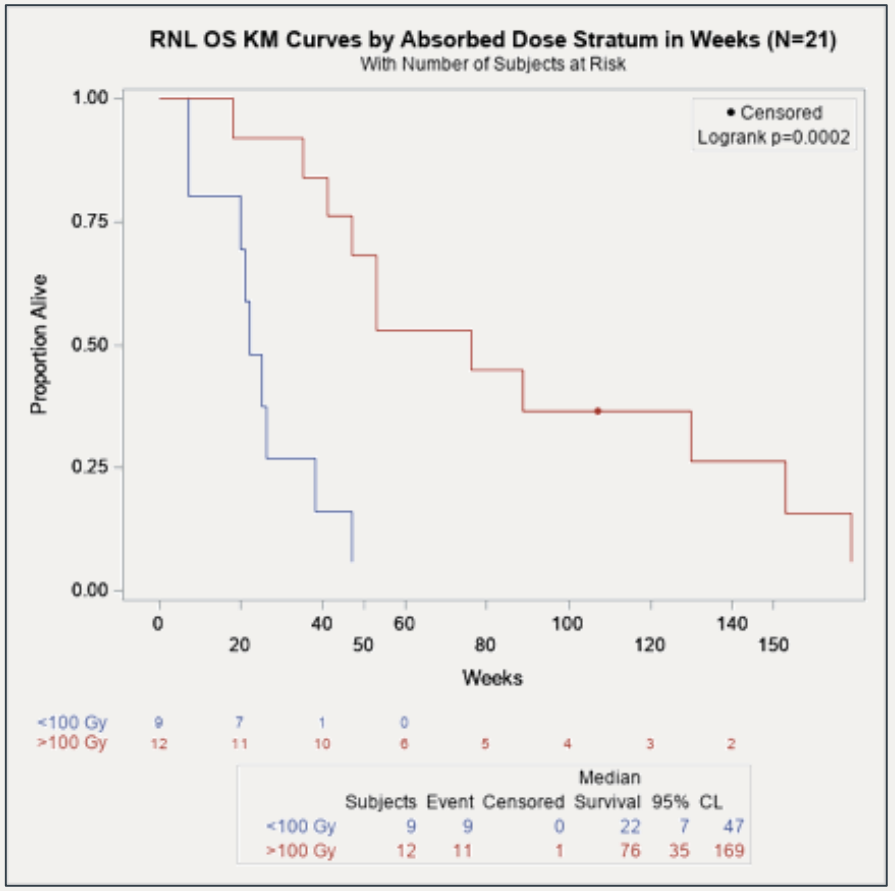
ReSPECT-GBM Trial for Recurrent Glioblastoma

Phase 1 efficacy data through RP2D determination (n=21 patients)

Overall Survival



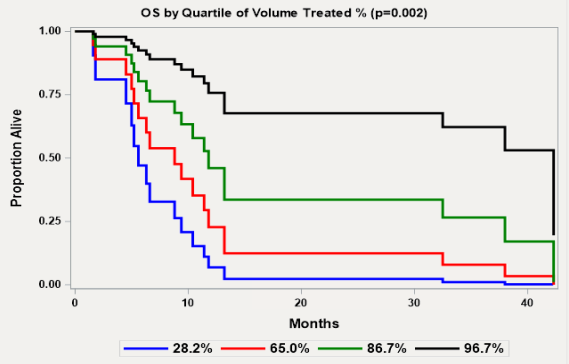
Overall Survival

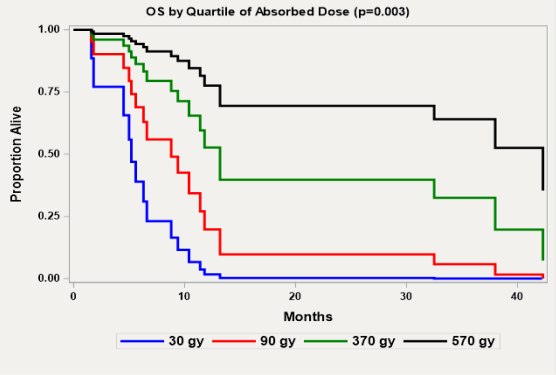


ReSPECT-GBM Trial for Recurrent Glioblastoma

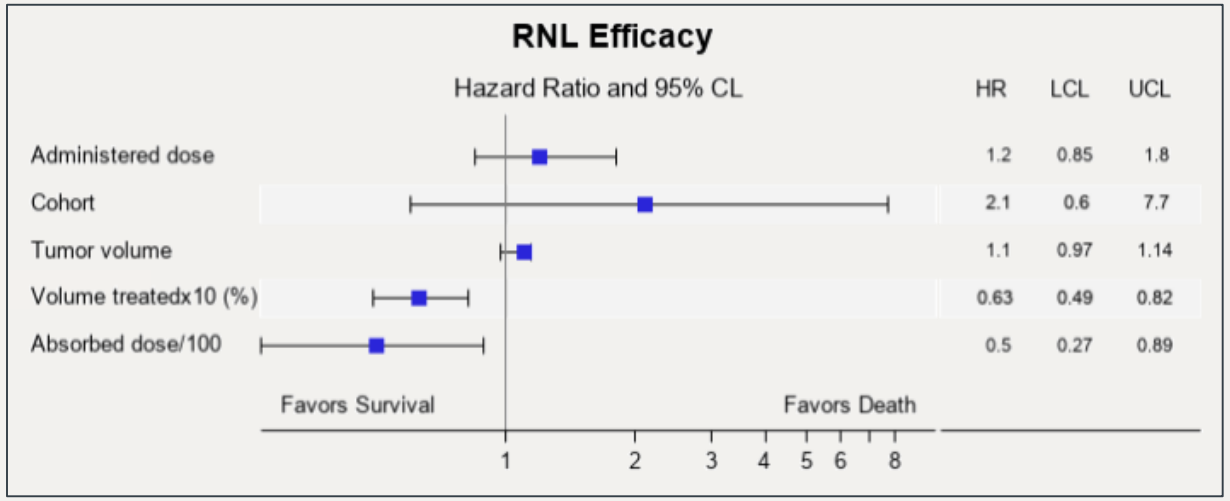
Phase 1 efficacy data through RP2D determination (n=21 patients)

Dose Response by Quartile





Hazard Ratio Model (Cox)



+ For each 100 Gy increase of Total Dose in Distribution Volume, the risk of death decreases by 45.6% (p=0.003)

+ For each 10% increase in the Ratio of Treated to Total Tumor Volume, the risk of death decreases by 66.9% (p=0.002)

Results

+ **Increased absorbed radiation dose** (p=0.003) and **percent tumor volume treated** (p=0.002) correlates with improvement in overall survival

+ Median OS in patients receiving > 100 Gy of absorbed dose was 76 weeks vs. 22 weeks if < 100 Gy (p=0.0002) compared to standard of care of 32.1 weeks in recent meta- analysis*

+ **Up to 20 times** the absorbed dose of EBRT delivered

+ Therapeutic absorbed radiation dose (>100 Gy) was reliably achieved in >**80% of patients treated in high dose cohorts**

**Neuro-Oncology*, 22(5), May 2020: 694–704, 705-717.
Oncol Lett, 14(1), Jul 2017: 1141–1146.

Comparative Survival Data

ReSPECT-GBM vs. 'Best' Real World Data

Trial or Data Source	Number Patients	Median Overall Survival
Meta-analysis*- Bevucizamab	~700	32.1 weeks (7 months)
MEDS- Bevacizumab	163	7.9 months
MEDS- CED	636	8.4 Months
ReSPECT-GBM Phase 1 Dose Escalation		
All	21	41 weeks (11 months)
<100Gy	9	22 weeks (6 months)
>100Gy	11	76 weeks (17 months)

**Neuro-Oncology*, Volume 22, Issue 5, May 2020, Pages 705–717
Neuro-Oncology, Volume 22, Issue 5, May 2020, Pages 694–704
Oncol Lett. 2017 Jul; 14(1): 1141–1146.

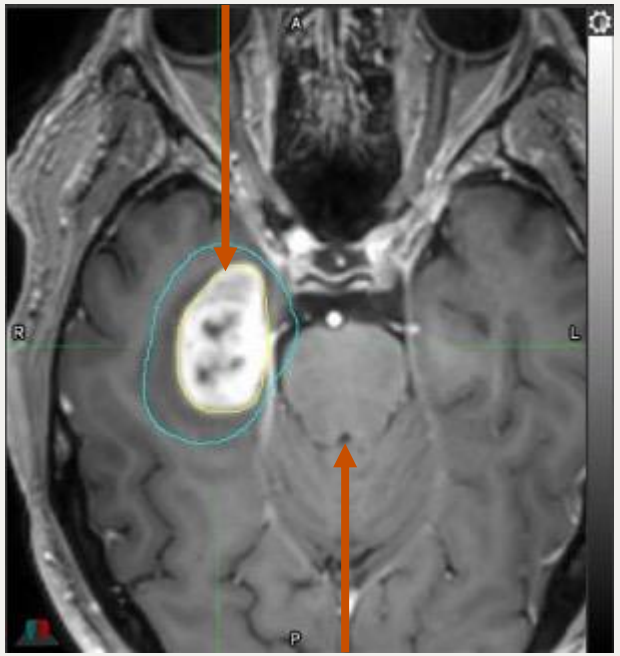
Medidata Enterprise Data Store (MEDS)

ReSPECT-GBM for Recurrent Glioblastoma

Phase 2 Case Study: Patient 02-004 – Imaging and Dosimetry

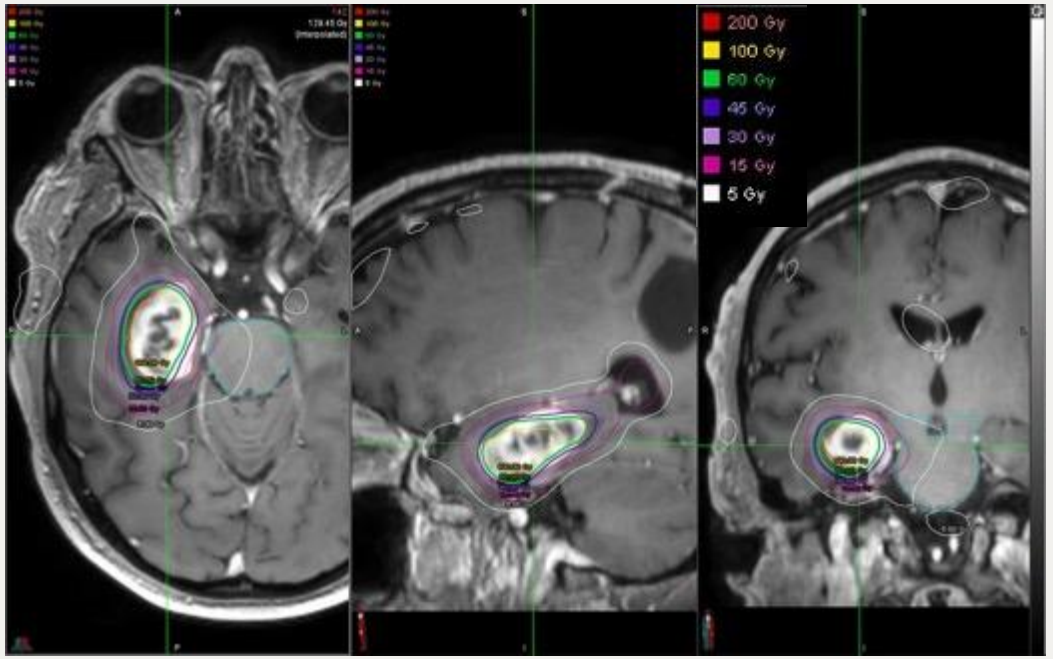
- Rapidly progressing, deep brain rGBM, adjacent to the brainstem
- 3 catheters used
- 8.8 mL infused volume, 22.3 mCi total injected radioactivity
- ^{186}RO tumor coverage at EOI: 94.6%
- Mean tumor dose: 105 Gy
- Patient alive at >100 days post treatment

Tumor volume: 9.58 mL



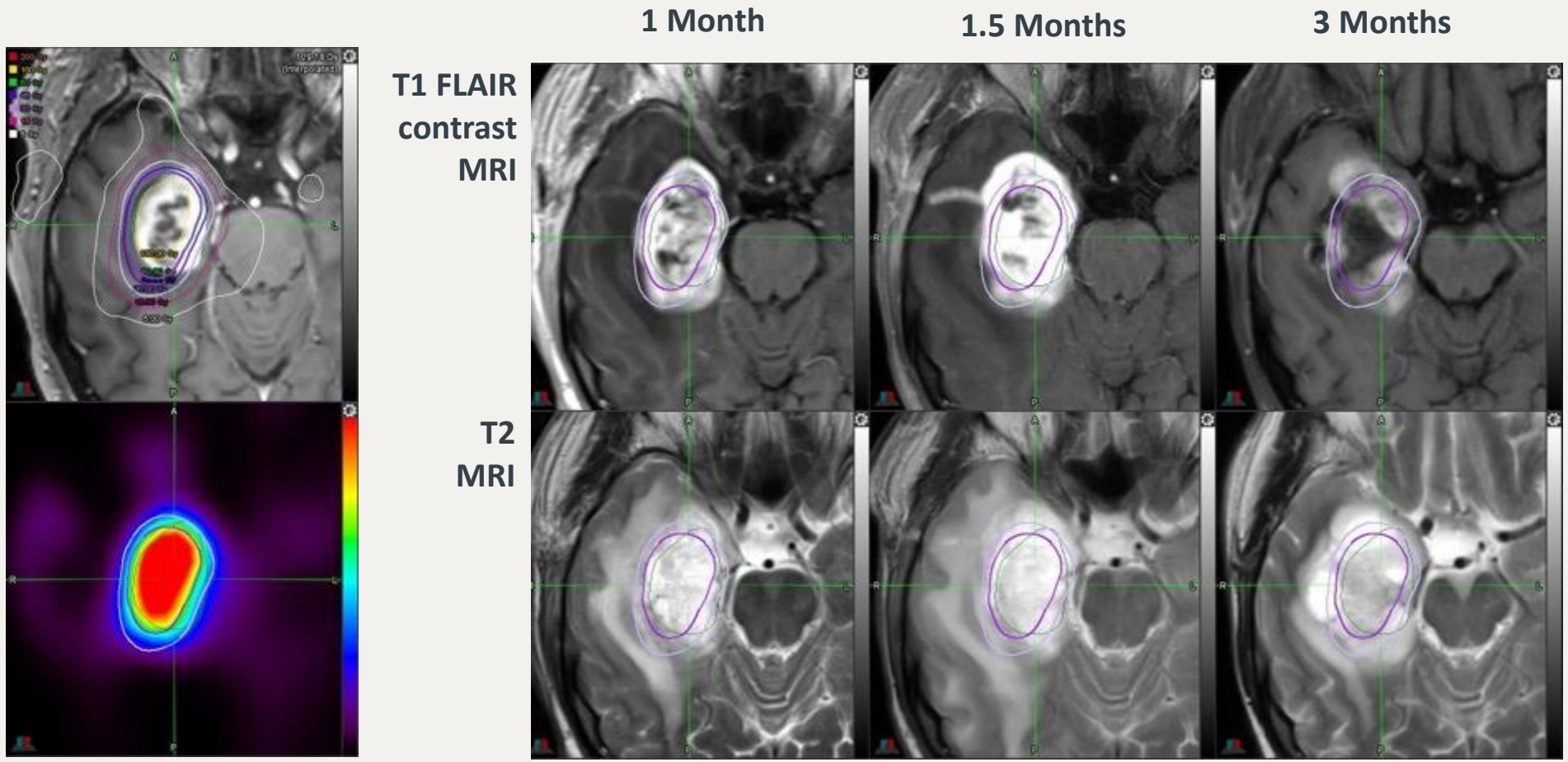
Brainstem

Dosimetry Analysis



ReSPECT-GBM for Recurrent Glioblastoma

Phase 2 Case Study: Patient 02-004 – Pre/Post Treatment MRI & SPECT



ReSPECT-GBM Phase 1 Trial Clinical Update

- A single dose of rhenium (186Re) obisbemeda was generally safe and well-tolerated, with no dose-limiting toxicities and minimal systemic radiation exposure.
- In 21 patient phase 1- efficacy signals observed in a prognostically unfavorable patient population.
- Median OS in all 21 patients (including those receiving very limited radiation doses in early cohorts, 5 Bev treated patients, etc.) was 11 months or 38% increase in survival vs. standard of care of ~8 months in rGBM.
- Median OS in patients receiving > 100 Gy of absorbed dose (therapeutic) was 76 weeks (17 mos) vs. 22 weeks (6 mos) if < 100 Gy (p=0.0002).
- Increased absorbed radiation dose and percent tumor volume treated best correlates with improvement in overall survival:
  - For each 100 Gy increase of Total Dose in Distribution Volume, the risk of death decreases by 45.6% (p=0.003).
  - For each 10% increase in the Ratio of Treated to Total Tumor Volume, the risk of death decreases by 66.9% (p=0.002).

- Headquarters: Austin, Texas
- Manufacturing: San Antonio, Texas
- Nasdaq: PSTV
- Corporate Website: PlusTherapeutics.com
- ReSPECT™ Website: ReSPECT-Trials.com

For more information on how to become involved with this trial, please contact:

Norman LaFrance, MD, ME, FACP, FACNP, FACNM

nlafrance@plustherapeutics.com