



# Corporate Presentation

Fall 2024

NASDAQ: PSTV



# Cautionary Note Regarding Forward Looking Statements

This presentation contains statements that may be deemed “forward-looking statements” within the meaning of U.S. securities laws, including statements regarding clinical trials, expected operations and upcoming developments. All statements in this presentation 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 “potential,” “anticipating,” “projecting,” “expecting,” “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. These statements include without limitation, statements regarding the following: the potential promise of <sup>186</sup>RNL, including the ability of <sup>186</sup>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, which include the Company’s nanomedicine platform and commercializing <sup>186</sup>RNL and 188RNL-BAM; the Company’s manufacturing capabilities and commercial scalability of the Company’s product candidates; the Company’s clinical trials including statements regarding the timing and characteristics of the ReSPECT-GBM, ReSPECT-LM, and ReSPECT-PBC clinical trials; possible negative effects of <sup>186</sup>RNL; the continued evaluation of <sup>186</sup>RNL, including through evaluations in additional patient cohorts; the intended functions of the Company’s platform and expected benefits from such functions; development and utility of the CNSide™ leptomeningeal metastases diagnostic test; and upcoming catalysts and cash runway.

The forward-looking statements included in this presentation 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 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 to fund its operations in the near term and long term, on terms acceptable to us or at all; the outcome of the Company’s partnering/licensing efforts; risks associated with laws or regulatory requirements applicable to the Company; market conditions; product performance; litigation or potential litigation; and 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; manufacturing and supply chain risks; 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, 2023, 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](http://www.sec.gov). Any or all forward-looking statements Plus Therapeutics makes may turn out to be wrong 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 presentation. Accordingly, you should not place undue reliance on the forward-looking statements made in this presentation, 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.

# Plus Therapeutics: Investment Highlights

Differentiated clinical stage targeted radiotherapeutics company

- + Clinical stage radiotherapeutics company focused on CNS cancers
- + Rhenium ( $^{186}\text{Re}$ ) represents a differentiated therapeutic radionuclide with favorable attributes for CNS (many cancers)
- + Incorporates clinically-proven drug delivery modalities
- + Nanoliposome-encapsulated radiotherapeutics achieved very high therapeutic index
- + Mature supply chain and straightforward last-mile logistics
- + Developing both first-in-class therapeutic and diagnostic/biomarker for leptomeningeal disease

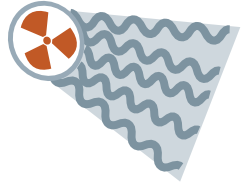
# Investigational Radiotherapeutics Pipeline

Lead Drug: Rhenium (<sup>186</sup>Re) Obisbameda a.k.a. Rhenium Nanoliposomes (<sup>186</sup>RNL)

Indication & Description		IND	Phase 1	Phase 2	Phase 3	Projected Milestones
<b>Leptomeningeal Metastases</b>	Single administration basket dose escalation trial	ReSPECT-LM Trial - <i>Single Dose</i>				<ul style="list-style-type: none"> <li>• Complete P1 LM single dose trial by Q1 2025</li> <li>• Initiate LM single dose expansion trial (P1b) in Q1 2025</li> </ul>
	Multi-dosing interval basket trial	ReSPECT-LM Trial - <i>Multi Dose</i>				<ul style="list-style-type: none"> <li>• Initiate enrollment Q1 2025</li> </ul>
<b>Recurrent Glioblastoma</b>	Large sized tumors	ReSPECT-GBM Trial				<ul style="list-style-type: none"> <li>• Complete – finalizing Clinical Study Report (CSR)</li> </ul>
	Small-to-medium sized tumors	ReSPECT-Recurrent GBM Trial				<ul style="list-style-type: none"> <li>• Complete by mid-2025</li> </ul>
<b>Pediatric Brain Cancer</b>	Pediatric high-grade glioma and ependymoma	ReSPECT-PBC Trial				<ul style="list-style-type: none"> <li>• Initiate enrollment in 2025</li> </ul>

# Background: Therapeutic Opportunities & Challenges in CNS Cancers

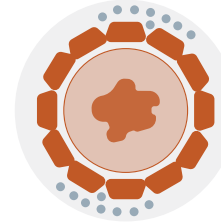
Radiation is the gold standard for CNS cancer therapy



## External Beam Radiation Therapy (EBRT) for CNS Cancers

Radiation is the best therapy for CNS cancers:

- + EBRT offers a survival benefit of 9-12 months for primary GBM (compared to 3-4 months for temozolomide and tumor-treating fields)<sup>1</sup>
- + Narrow therapeutic index of EBRT-limits dose due to off-target toxicity
- + Selective delivery of high-dose radiation to improve therapeutic index is practically challenging



## CNS Targeting is an Unsolved Problem

Multiple hurdles to development of targeted therapies to treat CNS cancers (i.e., antibodies, small molecules, etc.):

- + Blood-brain barrier
- + Immuno-protective environment
- + Low mutational load and no known driver mutations
- + Extensive activation of alternative pathways leads to rapid drug resistance

1. Chang JE, Khuntia D, Robins HI, Mehta MP. 2007. Radiotherapy and radiosensitizers in the treatment of glioblastoma multiforme. Clin Adv Hematol Oncol HO. 5(11):894-902, 907-915.

# Targeted Delivery of $^{186}\text{Re}$ RNL

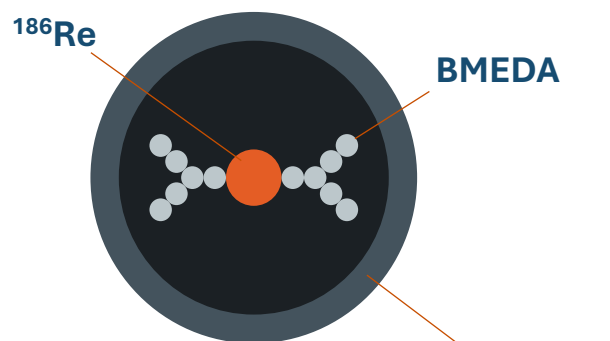
Potentially high therapeutic index for multiple CNS cancers

$^{186}\text{Re}$  RNL: Lead Investigational Drug

2 Delivery Modalities

Therapeutic Impact

Chelator (BMEDA) and Rhenium-186 Radionuclide  
(half-life = 90 hours)



Nanoliposome

Encapsulated in 100 Nanometer Liposome

CSF Malignancies  
Ex. LM



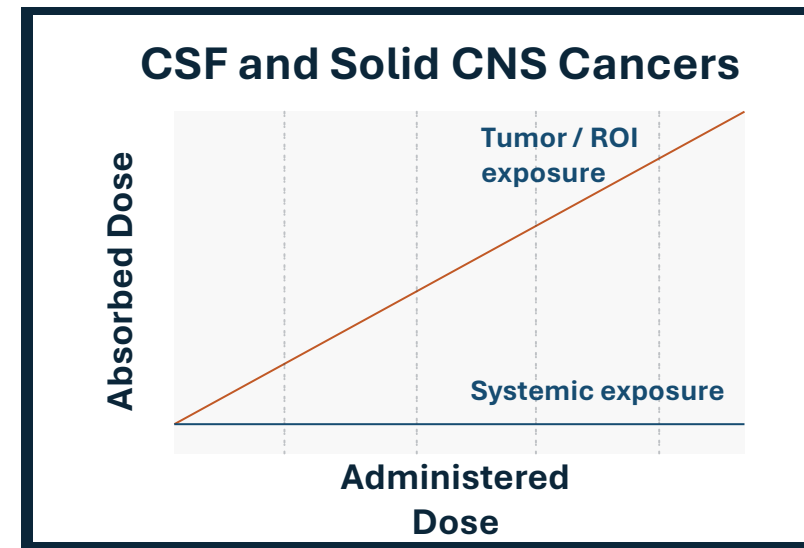
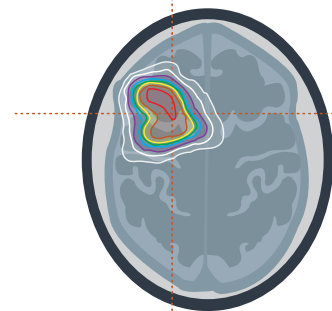
Intraventricular catheter (Ommaya reservoir)



Solid Tumors  
Ex. GBM



Convection Enhanced Delivery (CED)



Unique Marriage of Novel Agent & Drug Delivery Modality for CNS Cancers

May deliver up to 20x Gy vs EBRT without systemic toxicity

# Beta Emitter Rhenium-186 is a Differentiated Radionuclide

Chemistry, imaging, and tumoricidal characteristics optimal for CNS cancers

## Rhenium vs. Field

Optimal Features	$^{186}\text{Re}_{(\beta)}$	$^{225}\text{Ac}_{(\alpha \& \beta)}$	$^{212}\text{Pb}_{(\alpha)}$	$^{131}\text{I}_{(\beta)}$	$^{177}\text{Lu}_{(\beta)}$	$^{90}\text{Y}_{(\beta)}$
<b>Tumor Visualization</b> <i>Emits gamma particle</i>	✓	✓	✓			
<b>Treatment Depth</b> <i>2 mm avg path length</i>	✓					
<b>Optimal Tx Index</b> <i>Moderate KeV (~175-340 KeV)</i>	✓	✓	✓	✓		
<b>Optimal Tx Index</b> <i>Moderate half-life (<math>T_{1/2} = 90\text{h}</math>)</i>	✓			✓	✓	
<b>Optimal chemistry</b> <i>High-drug loading efficiency</i>	✓					

### EU Rhenium Experience

- + Extensive clinical data supports the safety and efficacy of rhenium<sup>1</sup>
- + Rhenium has been used safely and effectively for over 30 years in Europe to treat various cancers<sup>2</sup>

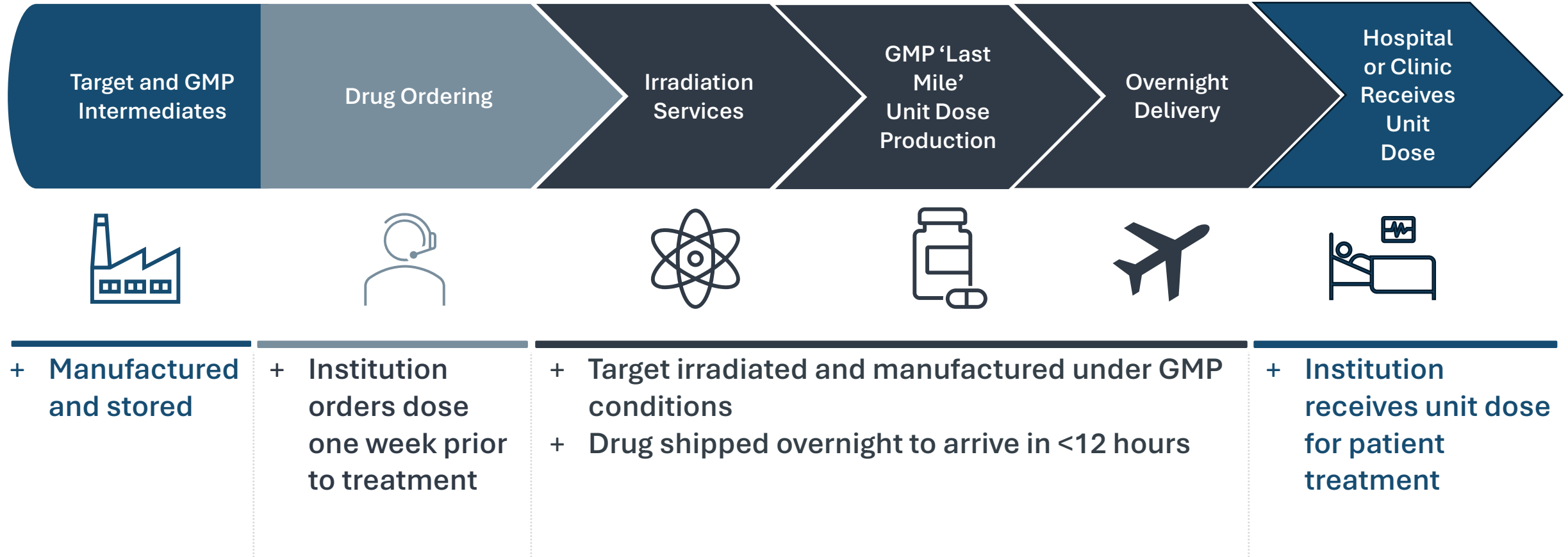
### $^{186}\text{Re}$ Decay

$^{186}\text{Re} = \text{beta particle} +$   
 $^{186}\text{Osmium} + \text{antineutrino}$

1. European Society for Medical Oncology (ESMO). "Rhenium-Based Therapies in Cancer Treatment,“; German Cancer Research Center (DKFZ), Innovations in Liver Cancer Treatment Using Rhenium.  
 2. Cancers include skin cancer, liver cancer, and bone metastases. Oncidium Foundation.

# <sup>186</sup>RNL Manufacturing- Scalable & Seamless Workflow

Company on track to supply all demand scenarios including commercial scalability





# Cerebrospinal Fluid (CSF) Malignancies

**Power and precision** in cancer  
radiotherapeutics



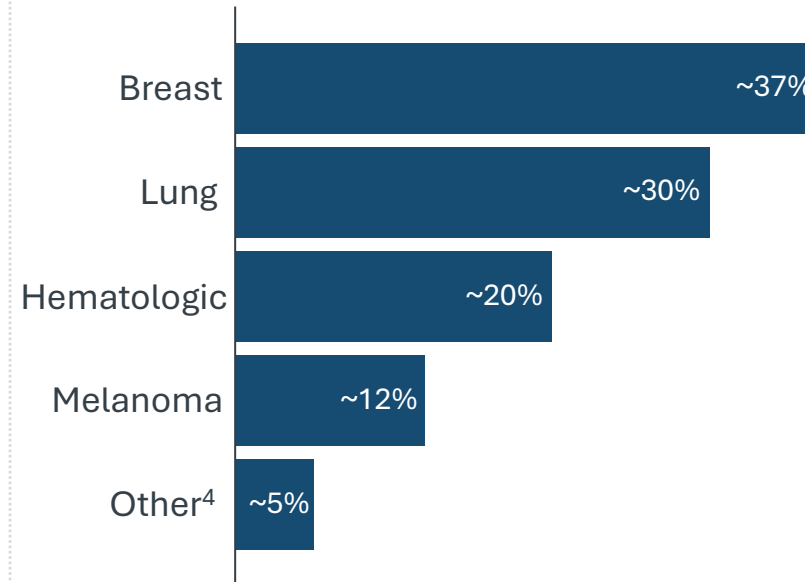
# CSF Malignancies: Leptomeningeal Metastases (LM)

Growing incidence with poor prognosis, inadequate diagnostics, and limited therapeutic options

## Growing & Unsolved Problem

- + Common cancers spread to the leptomeninges and cerebrospinal fluid space
- + Survival is poor: 4-6 weeks w/o Tx, 4-6 months with Tx
- + No approved therapies or standard of care
- + Only FDA approved drug Depocyt<sup>1</sup> no longer available
- + Randomized Phase 2 trial<sup>2</sup> suggests benefit with targeted radiation: proton CSI

## Common Primary Cancers<sup>3</sup>



## LM Underdiagnosed

Annual Incidence **110-130K<sup>3</sup>**

- + LM cases are likely 2-4x underdiagnosed based on autopsy findings<sup>1</sup>
- + Current diagnostic methods lack specificity and sensitivity (<50% sensitive for cytology)
- + Plus recently acquired highly sensitive circulating tumor cell diagnostic test should expand LM total addressable market for <sup>186</sup>RNL

1. Chamberlain M. C. (2012). Neurotoxicity of intra-CSF liposomal cytarabine (DepoCyt) administered for the treatment of leptomeningeal metastases: a retrospective case series. Journal of neuro-oncology, 109(1), 143–148. <https://doi.org/10.1007/s11060-012-0880-x>

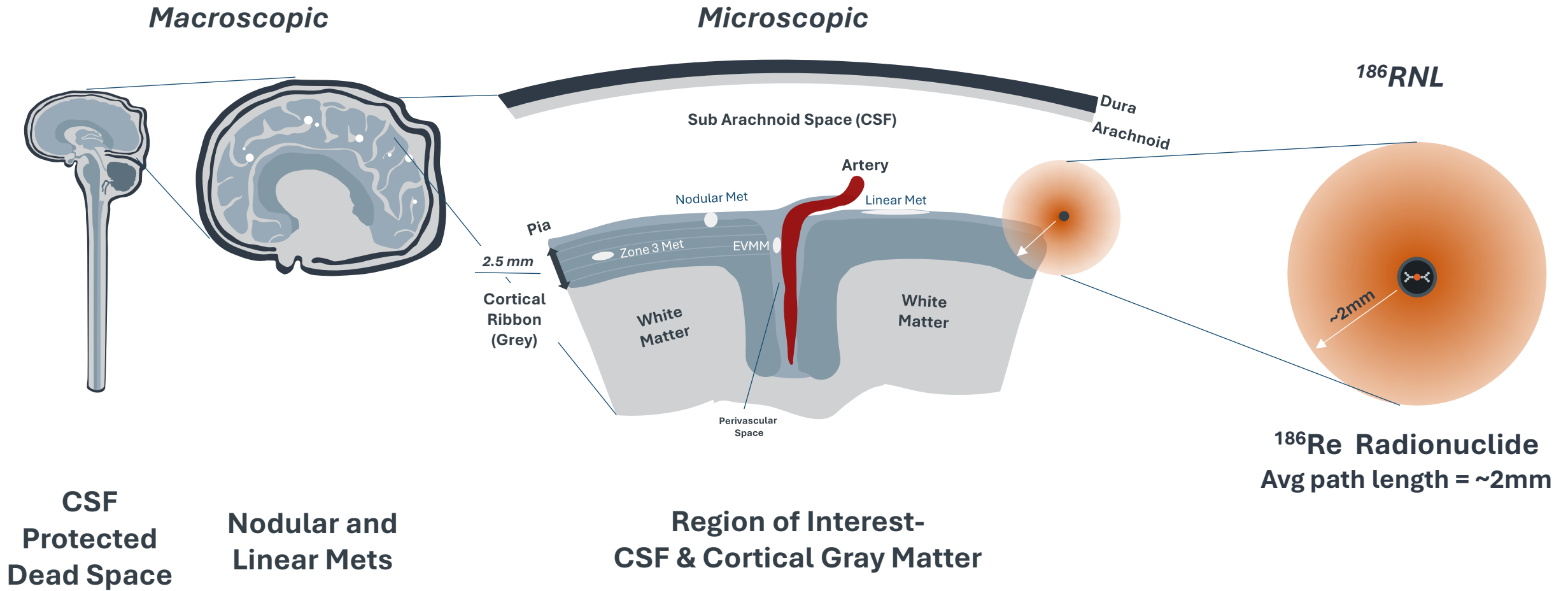
2. J Clin Oncol 40:3858-3867

3. See Appendix; based on 15+ independent studies across 1,700+ patients diagnosed with LM

4. Other primary cancers include primary brain tumors, prostate cancer, GI cancers, lymphoma, leukemia

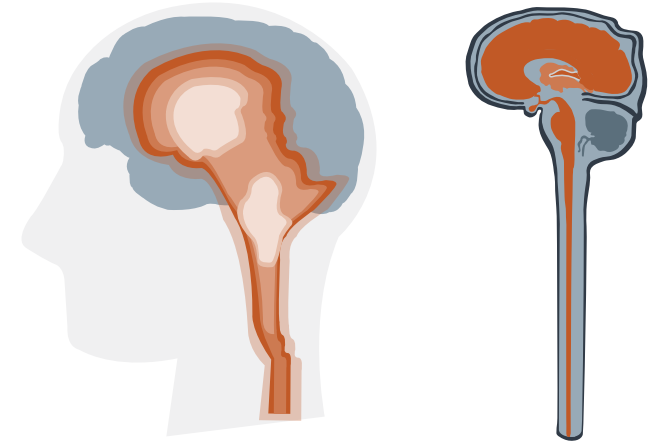
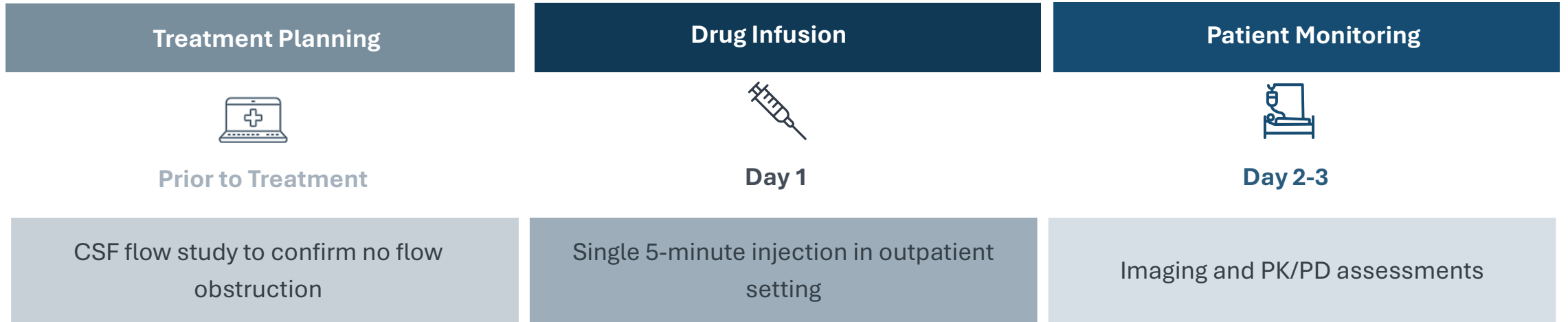
# Pathology of Leptomeningeal Disease Drives Therapeutic Approach

Rhenium-186 energy profile and pathlength treats unique CNS anatomy & region of interest



# <sup>186</sup>RNL Treatment Workflow for LM

Single administration analogous to intrathecal chemotherapy



# ReSPECT-LM Phase 1 Single Administration Dose Escalation Trial

Trial design: single administration delivery via standard Ommaya reservoir

- + **Dose escalation:** 3+3 modified Fibonacci
- + **Primary objective:** Safety and tolerability
  - + Maximum Tolerated Dose (MTD) / Maximum Feasible Dose (MFD) via Ommaya reservoir
- + **Secondary objectives:** Efficacy
  - + Overall Response Rate (ORR)
  - + Duration of Response (DoR)
  - + Progression Free Survival (PFS)
  - + Overall survival (OS)
- + **Other objectives:** Analysis on CSF, pK
  - + CSF circulating tumor cells (CTCs)
  - + Pharmacodynamic (PD) markers & dosimetry
- + **Funding:** \$17.6M grant from largest state funder of cancer research in U.S. (CPRIT)

Cohort	Administered Volume (mL)	Administered Activity (mCi)	Administered Concentration (mCi/mL)
1	5	6.6	1.32
2	5	13.2	2.64
3	5	26.4	5.28
4	5	44.10	8.82
5	5	66.14	13.23
6	5	75.0	15.00
7	5	109.96	21.99

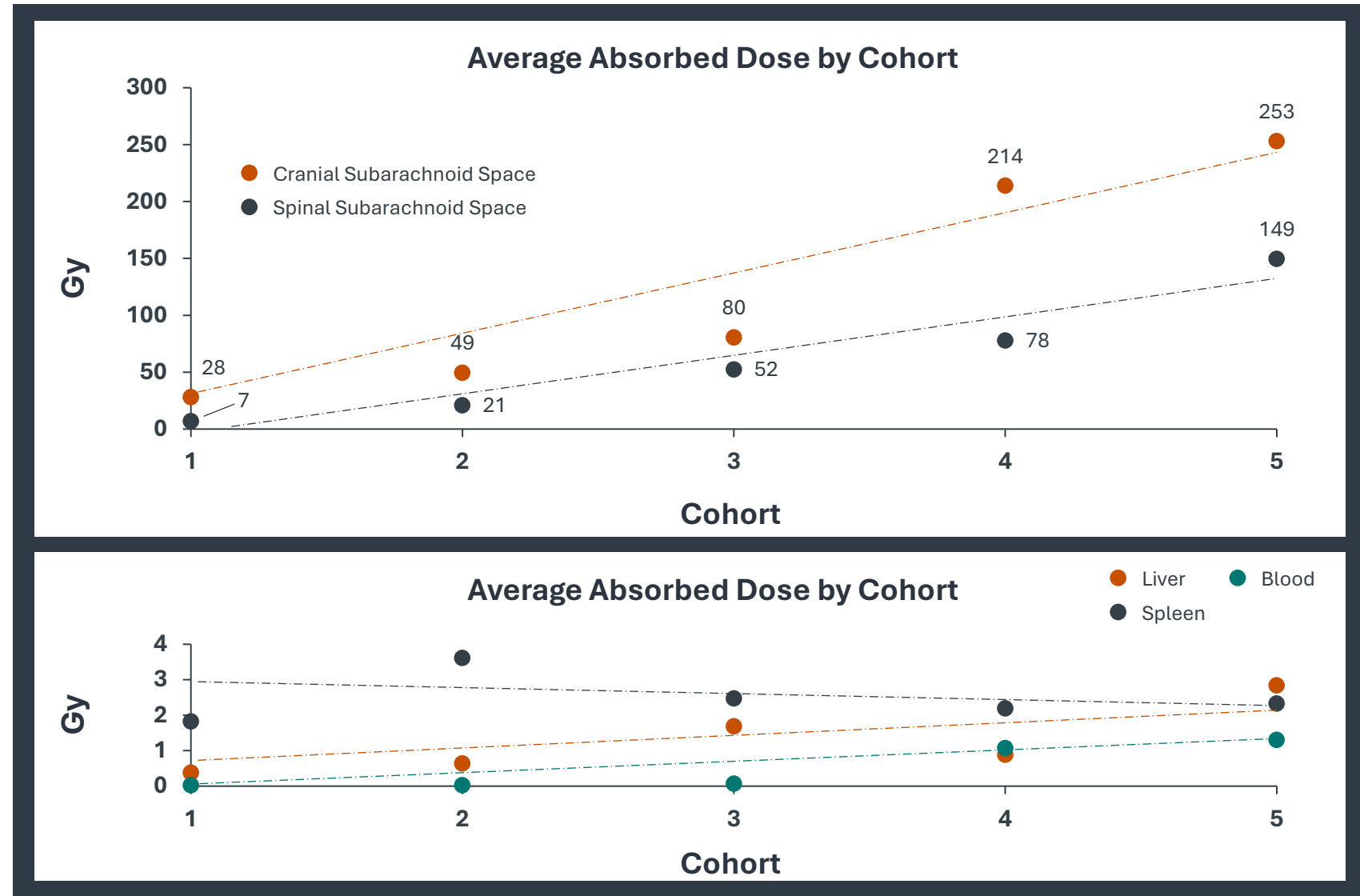


CANCER PREVENTION & RESEARCH  
INSTITUTE OF TEXAS

# ReSPECT-LM Phase 1 Single Administration Dose Escalation Trial

Dosimetry & pK shows linear increase in absorbed & limited systemic dose

- + Target/off-target radiation absorbed dose ratio >100/1
- + Low radiation exposure to critical organs
- + Radiation measured in CSF space for 7 days
- + Complete CSF circulation of drug seen by 3.5-hour imaging timepoint
- + **General toxicity limits<sup>1</sup>:**
  - + Liver: ~35-50 Gy
  - + Spleen: ~40 Gy
  - + Bone marrow: ~2-5 Gy



1. J Nucl Med. 2021 Dec;62(Suppl 3):23S-35S. doi: 10.2967/jnumed.121.262751.

# ReSPECT-LM Phase 1 Single Administration Dose Escalation Trial

Safety summary shows  $^{186}\text{Rn}$  well tolerated through Cohort 5

P1 Single Administration Dose Escalation						
N = 20 evaluable						
Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	<b>Cohort 6</b>	Cohort 7
6.6	13.2	26.4	44.1	66.1	<b>75</b>	110
mCi	mCi	mCi	mCi	mCi	<b>mCi</b>	mCi

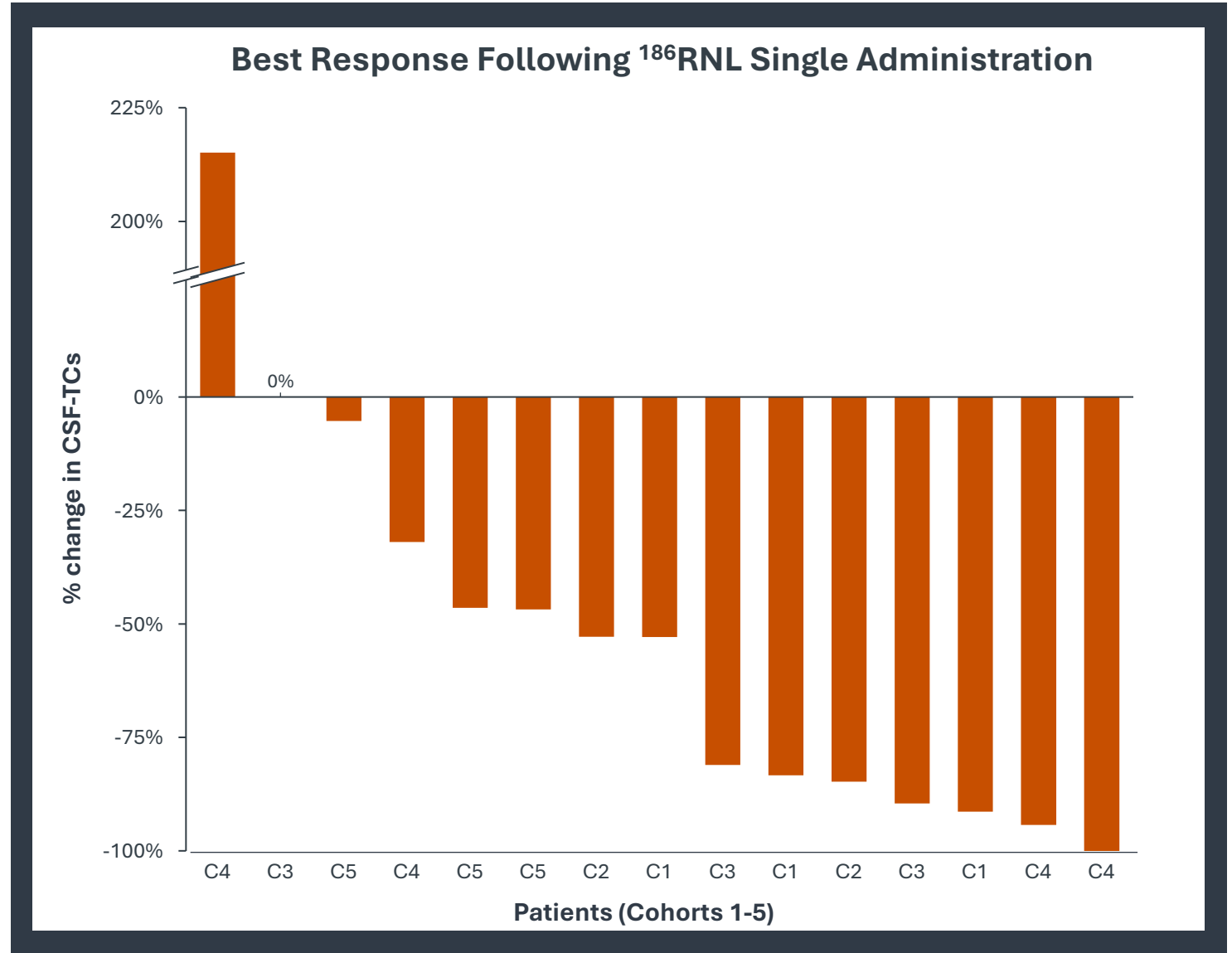
- + N = 33 enrolled, 7 screen failures, 26 intent to treat, 20 per treatment evaluable, 1<sup>st</sup> patient treated in Cohort 6
- + A single DLT noted thus far at 66.14 mCi administered dose (thrombocytopenia)
- + Adverse Events
  - + Most common AEs (>20% of patients): headache, vomiting, nausea
  - + Most AEs mild (grade 1, 60%) and moderate (grade 2, 28%)
  - + Most AEs unrelated (38%) or unlikely related (28%) to study drug
  - + Two AEs (headache) deemed definitely related to study drug (1 was grade 3 and resolved with treatment)
- + Serious Adverse Events
  - + 17 SAEs (7% of AEs)
  - + 3 SARs<sup>1</sup> (SAEs with at least 'possible' attribution) – (1) encephalopathy (also attributed to steroid taper, resolved spontaneously), (2) headache (resolved with treatment), and (3) thrombocytopenia (resolved with treatment)

1. Serious adverse reaction

# ReSPECT-LM Phase 1 Single Administration Dose Escalation Trial

Best response in tumor cells (CTCs) vs. baseline

- + National Comprehensive Cancer Network (NCCN) guidelines recommends CSF CTCs for Dx and disease monitoring in LM
- + Response in CSF CTCs following  $^{186}\text{RnL}$  treatment:
  - + 1/15 showed complete response
  - + 12/15 showed partial response





# ReSPECT-LM Phase 1 Single Administration Dose Escalation Trial

Combined best response vs. baseline after single administration – through 4 months

## + Clinical Benefit Rate (CR+PR+SD)

- + CTC response: 93% (14/15)
- + MRI Imaging response: 75% (12/16)
- + Clinical response: 86% (12/14)

Single dose response assessed from pretreatment through 4 months (112 days) follow-up							
Response Measure <sup>1</sup>	Response	Stable Disease	Clinical Benefit Rate	Progression	Evaluable Patients	Data Not Available	Total Patients
<b>CTC</b>	13	1	14	1	15	5	20
<b>Imaging</b>	5	7	12	4	16	4	20
<b>Clinical</b>	2	10	12	2	14	6	20

**CR** = Complete response  
**PR** = Partial response  
**SD** = Stable disease  
**CTC** = Circulating tumor cells

1. EANO-ESMO response criteria in LM includes: cytology, imaging & clinical evaluation

# ReSPECT-LM Phase 1 Single Administration Dose Escalation Trial

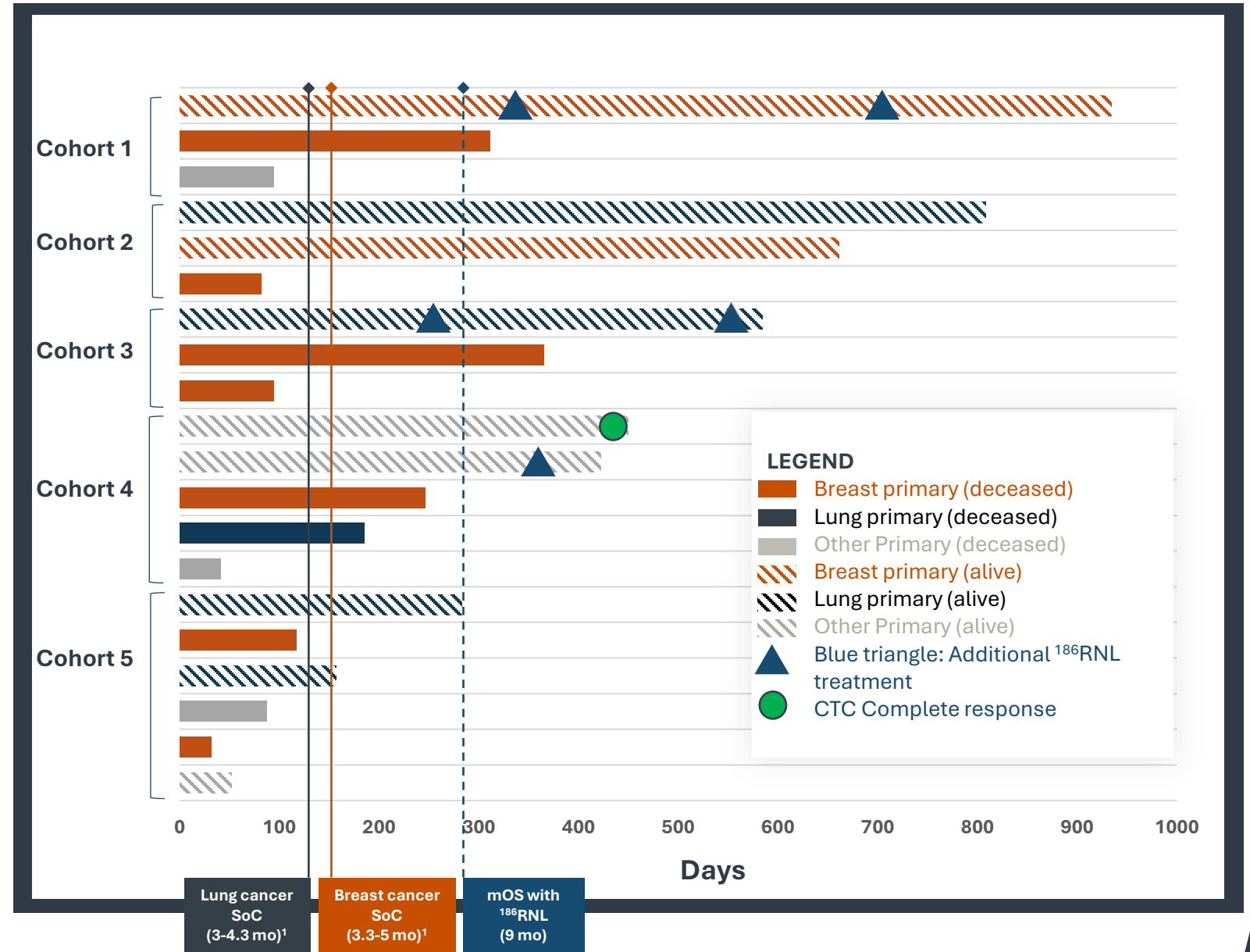
Swimmer's plot shows survival by cohort & primary cancer

## Analysis by primary cancer and survival time in the dose escalation phase

- + n = 20 evaluable patients
- + 9 patients alive at analysis
- + Tumors by primary disease
  - + Breast: 9
  - + Lung: 5
  - + Other: 6

## Key point

- + Multiple long-term survivors, including those receiving multiple doses through compassionate use

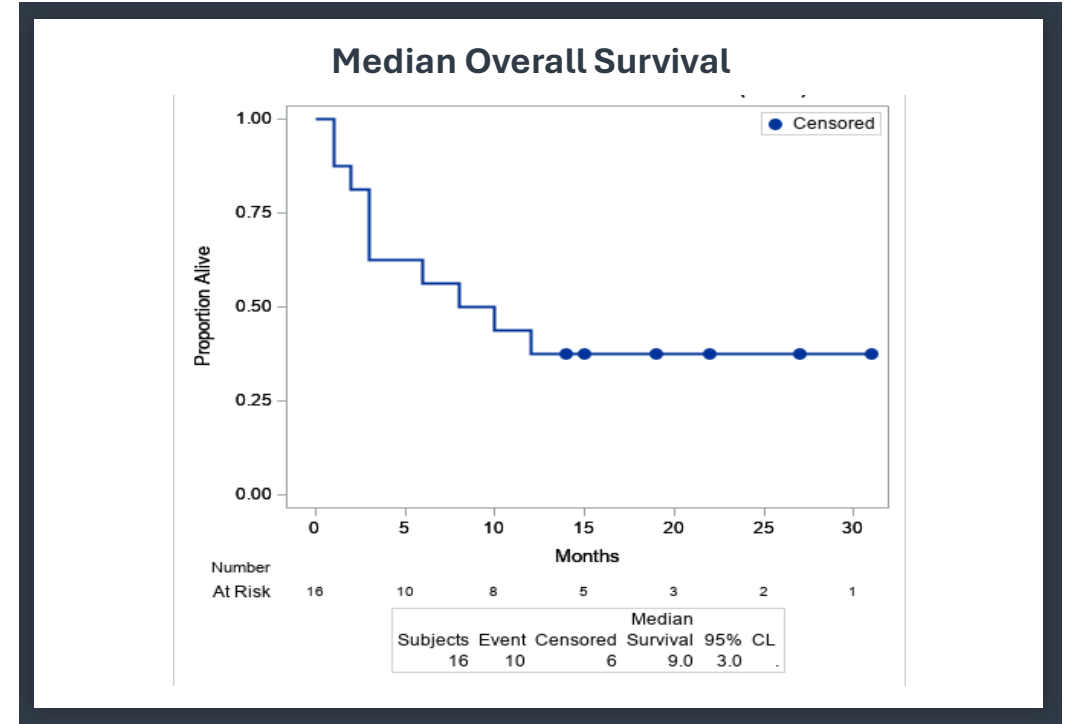


1. Le Rhun E, et al. Surg Neurol Int 2013;4:S265-88.

# ReSPECT-LM Phase 1 Single Administration Dose Escalation Trial

Median overall survival of 9 months through Cohort 4

- + Positive mOS signal in dose escalation phase
- + mOS of 9 months, compared to 4-6 months reported survival
- + n = 16 patients, Cohorts 1-4
- + 6 patients remain alive at analysis<sup>1</sup>



1. As of Nov 15, 2024

# Current Clinical Investigational Plan for <sup>186</sup>RNL in LM

Bayesian design evaluating both single and multiple dosing regimes in parallel

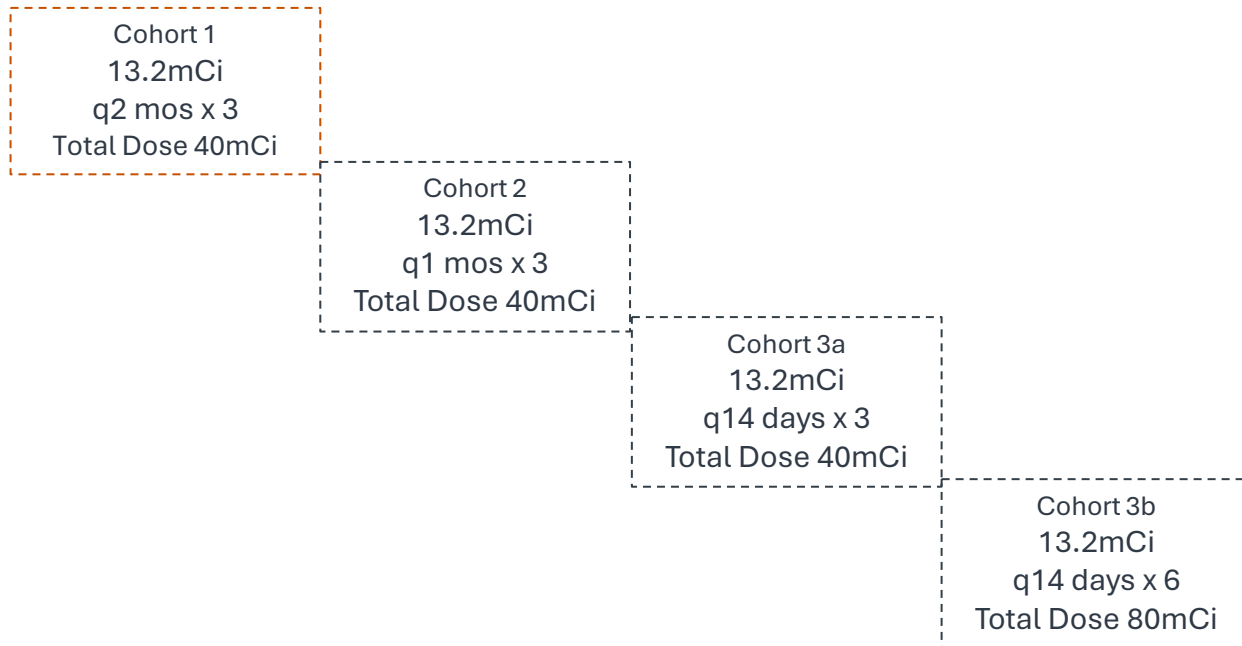
## P1 Single Administration Dose Escalation

Cohort 1 6.6 mCi	Cohort 2 13.2 mCi	Cohort 3 26.4 mCi	Cohort 4 44.1 mCi	Cohort 5 66.1 mCi	<b>Cohort 6 75 mCi</b>	Cohort 7 110 mCi
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P1b Single Dose Expansion Cohort  
(Breast & NSCLC)

## P1 Multiple Administration Dose Frequency



P2/3  
Registrational Trial



P1b Multiple Dose Expansion Cohort  
(Breast & NSCLC)

# Cerebrospinal Fluid Malignancies: LM

## + Summary

- + Reliable delivery modality with  $^{186}\text{RnL}$  allows treatment of entire region of interest: CSF dead space, leptomeninges & cortical grey matter
- + Favorable PK: single dose  $^{186}\text{RnL}$  typically remains in CSF for at least 7 days
- + High dose radiation to CSF with minimal systemic toxicity
- + Ongoing LM single administration basket dose escalation trial shows safety, feasibility, response, and favorable efficacy signal

## + Next Steps and Expected Milestones

- + Complete P1 LM single dose trial by Q1 2025
- + Initiate LM single dose expansion trial (P1b) in Q1 2025
- + Initiate enrollment in LM multi-administration dose interval compression trial by Q1 2025

# Solid CNS Malignancies

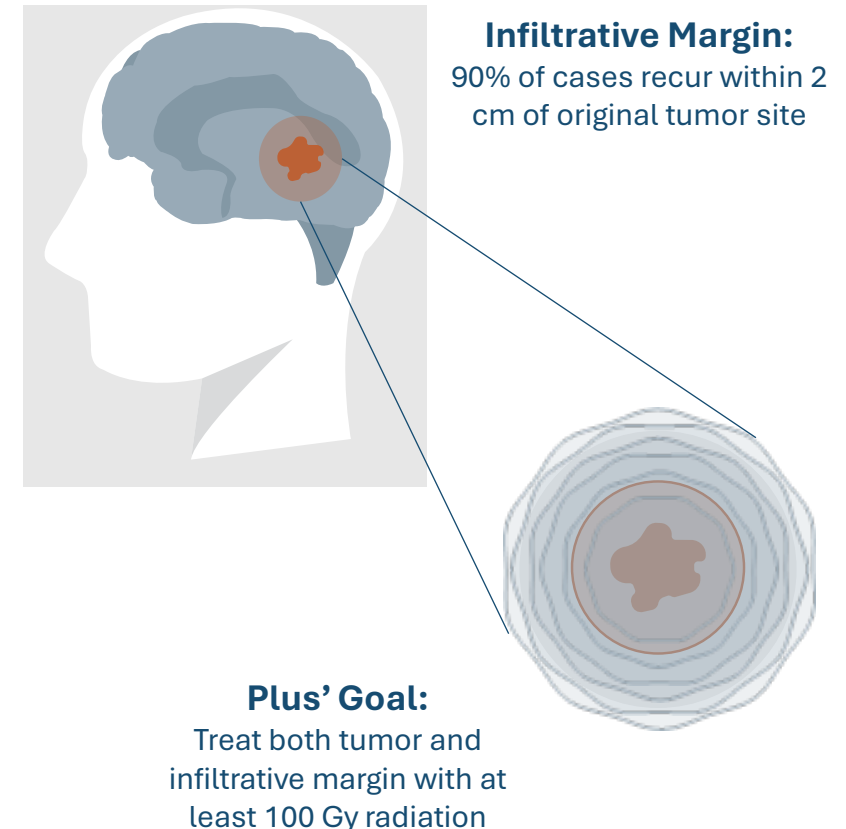
**Power and precision** in  
cancer radiotherapeutics



# Malignant Gliomas

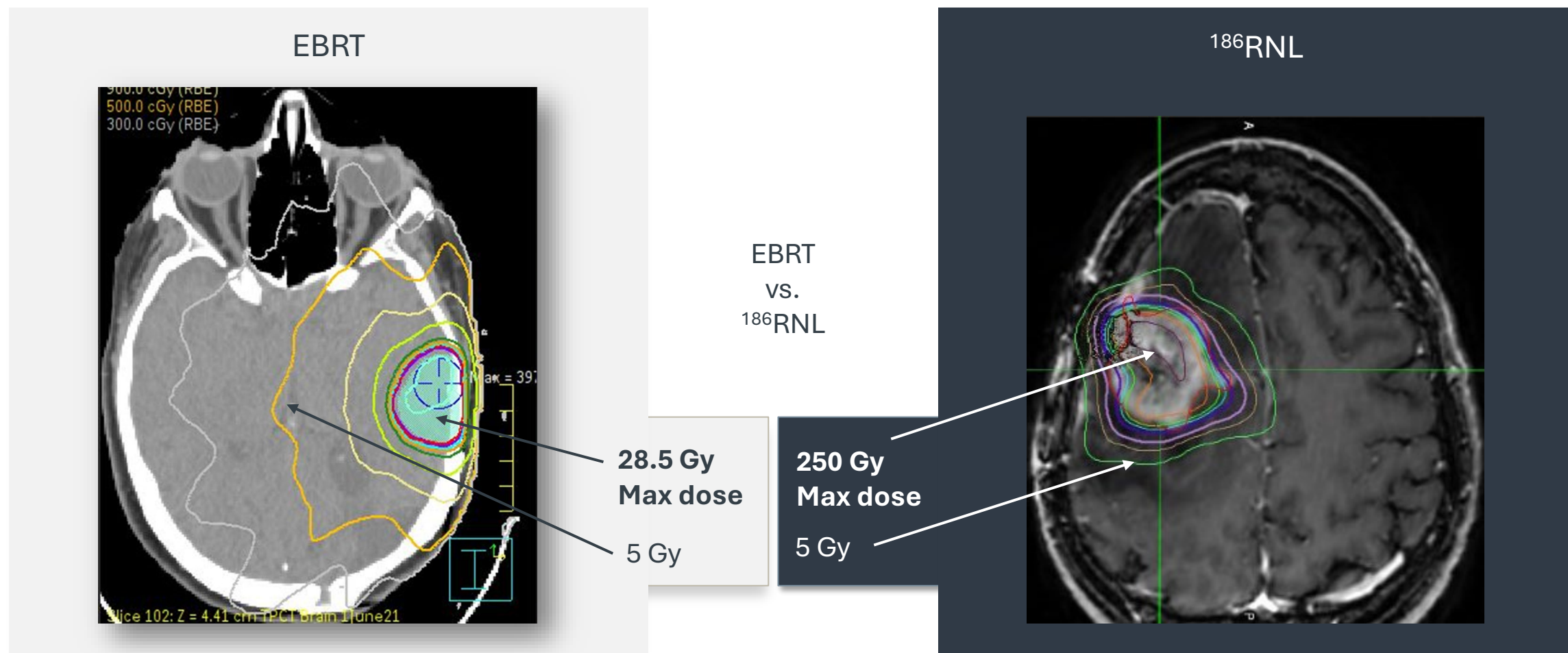
Aggressive and deadly disease, resistant to conventional treatments despite extensive research

- + **GBM is the most prevalent malignant tumor affecting the brain and central nervous system**
  - + ~15,000 patients newly diagnosed GBM patients in U.S. each year<sup>1</sup>
- + **Large unmet medical need for GBM patients**
  - + Poor survival rate (7% at 5 years after diagnosis)
  - + Almost all reoccur after several months post treatment or respond poorly to initial treatment
  - + No standard of care following recurrence, clinical trials recommended
  - + **GBM infiltrative margin must be addressed to achieve better outcomes**



# $^{186}\text{RNL}$ Advantage vs. Gold Standard EBRT

More targeted radiation delivery with 10-20x increase in maximum absorbed dose vs. EBRT

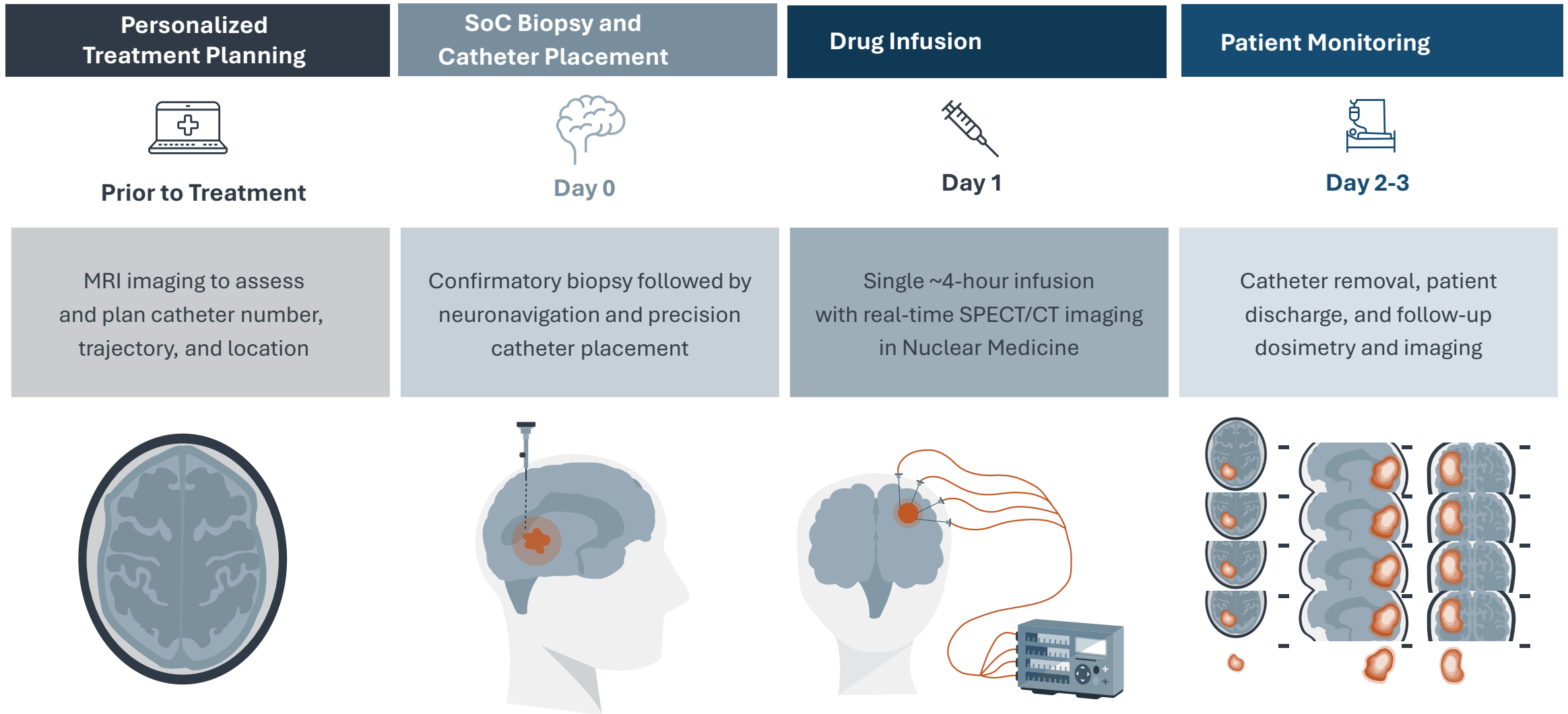


$^{186}\text{RNL}$  can deliver >100 Gy radiation to tumor and infiltrative margin



# $^{186}\text{RnL}$ Treatment Workflow in Brain Tumors Such As Recurrent GBM

Workflow similar to standard brain biopsy with catheters left in overnight for CED



# ReSPECT-GBM Phase 1 Single Administration Dose Escalation Trial

Trial design: single administration of  $^{186}\text{RnL}$  by Convection Enhanced Delivery (CED)

- + **Dose escalation:** 3+3 modified Fibonacci, currently enrolling in cohort 8
- + **Primary objective:** Safety and tolerability
  - + Maximum Tolerated Dose / Maximum Feasible Dose
- + **Secondary objectives:** Efficacy
  - + Dose distribution
  - + Overall Response Rate (ORR)
  - + Progression Free Survival (PFS)
  - + Overall survival (OS)
  - + Imaging
- + **Funding:** NIH/NCI grant through Phase 2

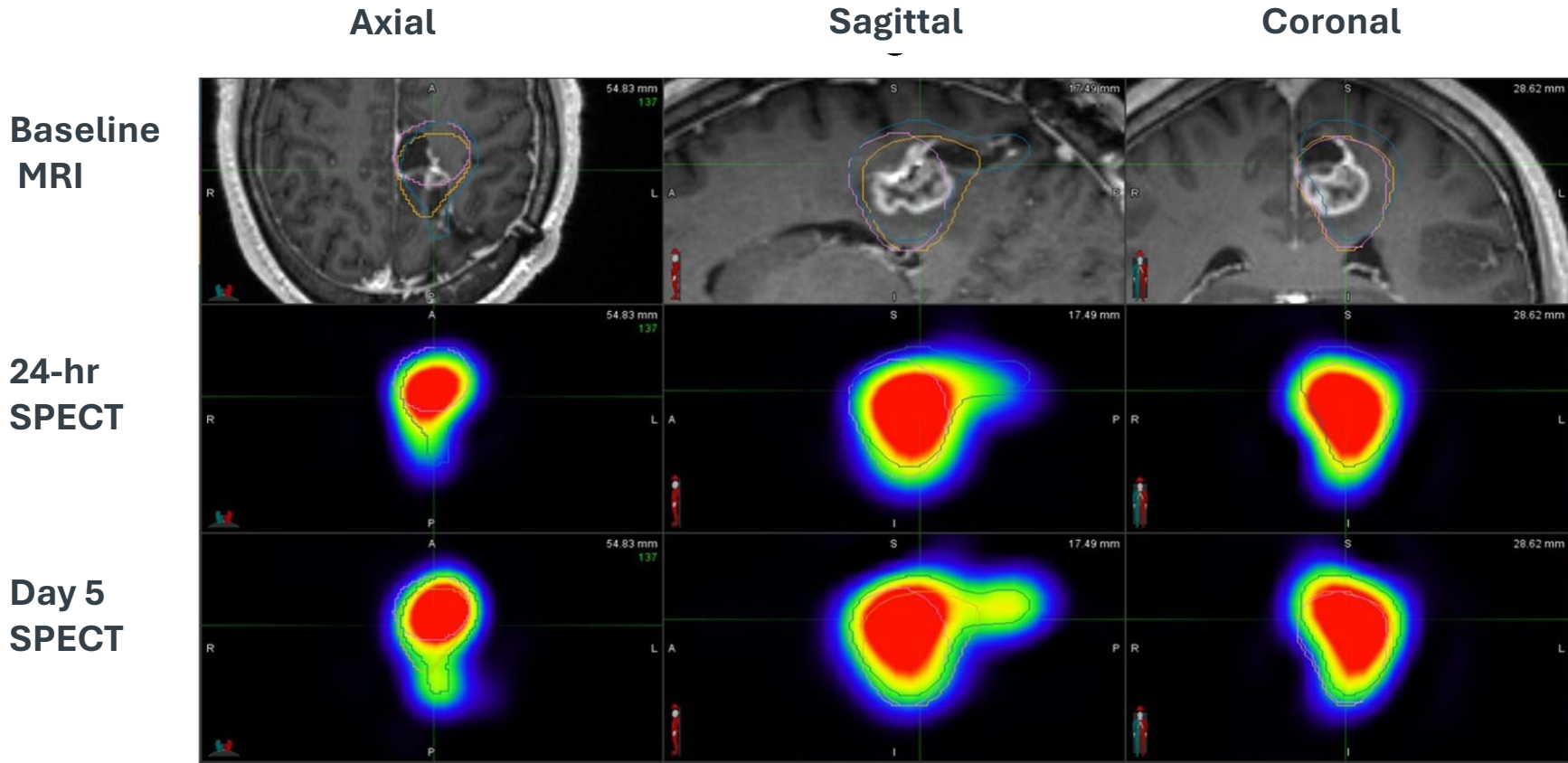
Cohort	Administered Volume (mL)	Administered Activity (mCi)	Administered Concentration (mCi/mL)
1	0.66	1.0	1.5
2	1.32	2.0	1.5
3	2.64	4.0	1.5
4	5.28	8.0	1.5
5	5.28	13.4	2.5
6	8.80	22.3	2.5
7	12.3	31.2	2.5
8	16.34	41.5	2.5



# ReSPECT-GBM Phase 1 Single Administration Dose Escalation Trial

Precision delivery & long-term retention of  $^{186}\text{Re}$  obtained via single procedure

## Patient 01-014



- + **Tumor Size: 6.5 mL**
- + **Percent tumor coverage: > 90%**
- + **Average absorbed Radiation dose: 419 Gy**

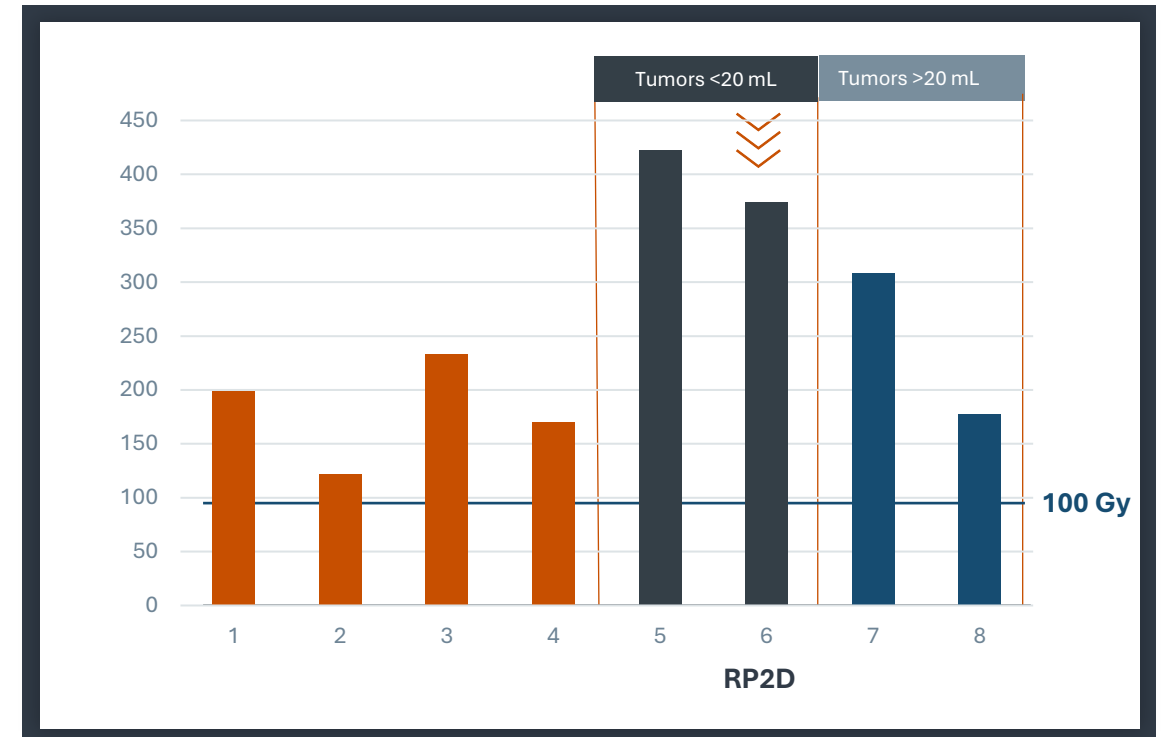
# ReSPECT-GBM Phase 1 Single Administration Dose Escalation Trial

Favorable safety signal in Phase 1/2 and selection of RP2D for small to medium tumor sizes (20 mL or less)

Phase 1 Safety Summary			
Grade	%	Most common AEs	SAEs
Grade 1	65.7%	Headache Fatigue	18
Grade 2	25.2%		(only 2 possibly related)
Grade 3	6.5%		
Grade pending	2.6%		

- + Generally safe and well tolerated over 29 patients in 8 Phase 1 dosing cohorts
- + 1 DLT in cohort 8 (hemiplegia)
- + Most Phase 1 adverse events (AEs) were mild/moderate, unrelated/unlikely related to study drug, and resolved with treatment
- + Increasing tumor size lowers average absorbed dose (cohorts 7 and 8)
- + 19 (out of 34) patients treated at the RP2D
- + Phase 2 safety profile consistent with Phase 1 data

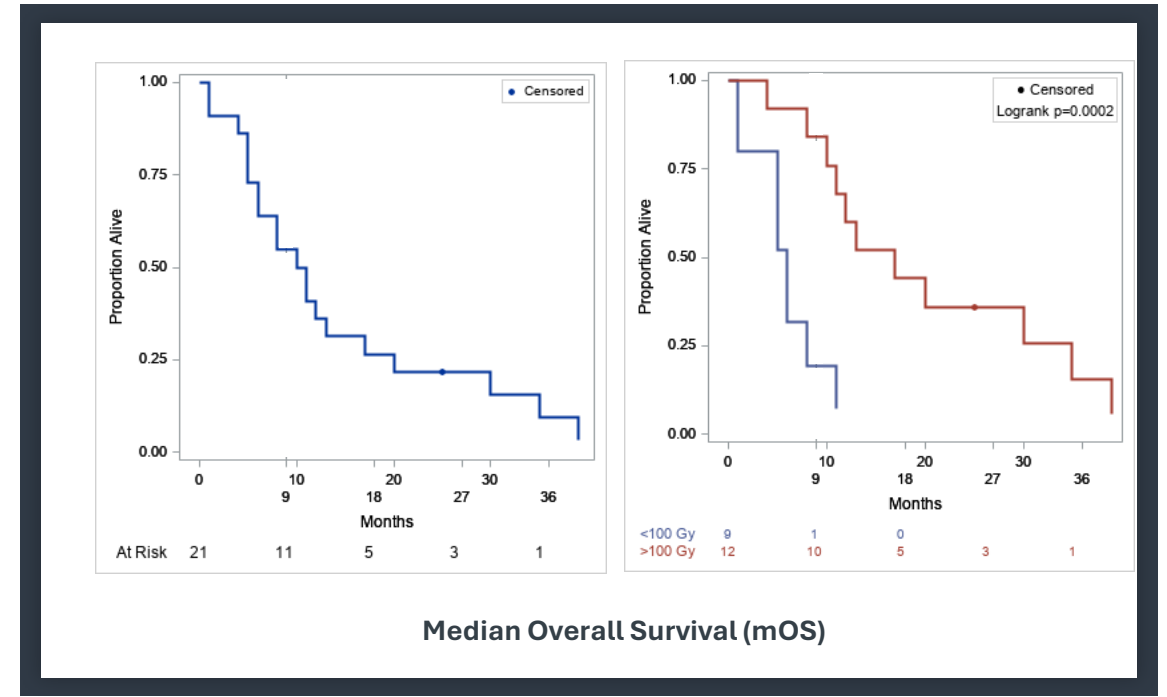
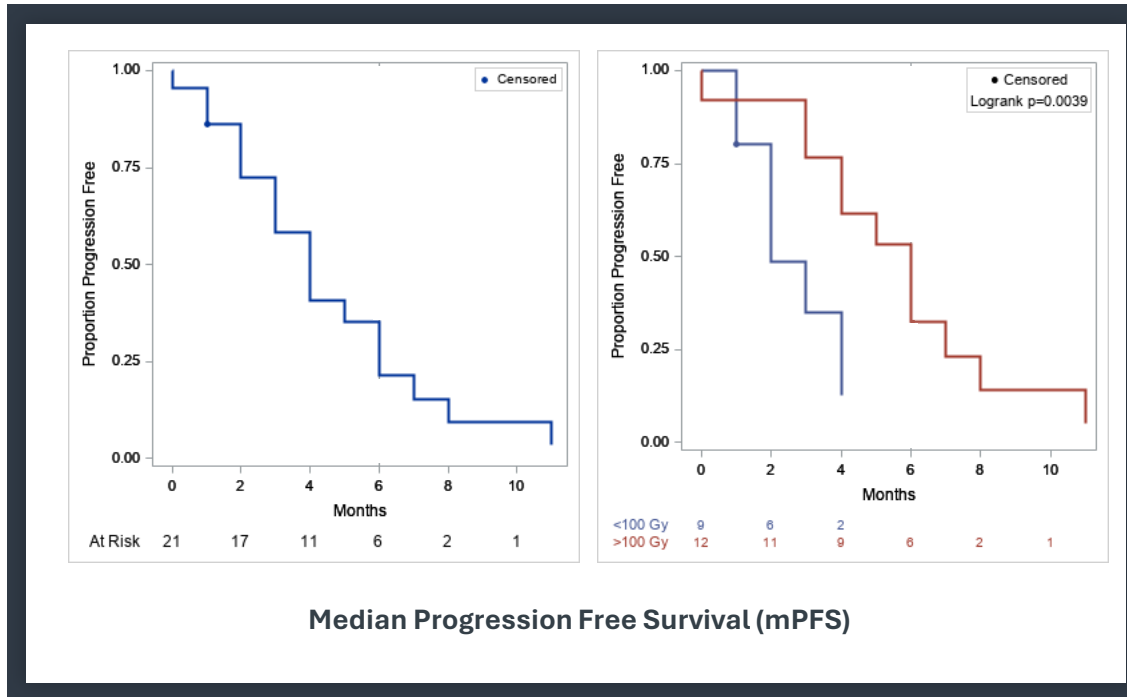
### Average Absorbed Dose to Tumor by P1 Cohort



- + The average absorbed dose to the tumor for all Phase 1 patients was 258 Gy (range: 8.9-739.5 Gy)
- + P2 average absorbed dose to the tumor (n=19) of 300 Gy to date

# ReSPECT-GBM Phase 1 Single Administration Dose Escalation Trial

Statistically significant survival benefit in patients meeting or exceeding delivery 'threshold' parameters



- + All patients: 4.0 months
- + <100 Gy: 2.0 months (blue)
- + ≥100 Gy: 6.0 m (red)

- + All patients: 11.0 months
- + <100 Gy: 6.0 months (blue)
- + ≥100 Gy: 17.0 months (red)



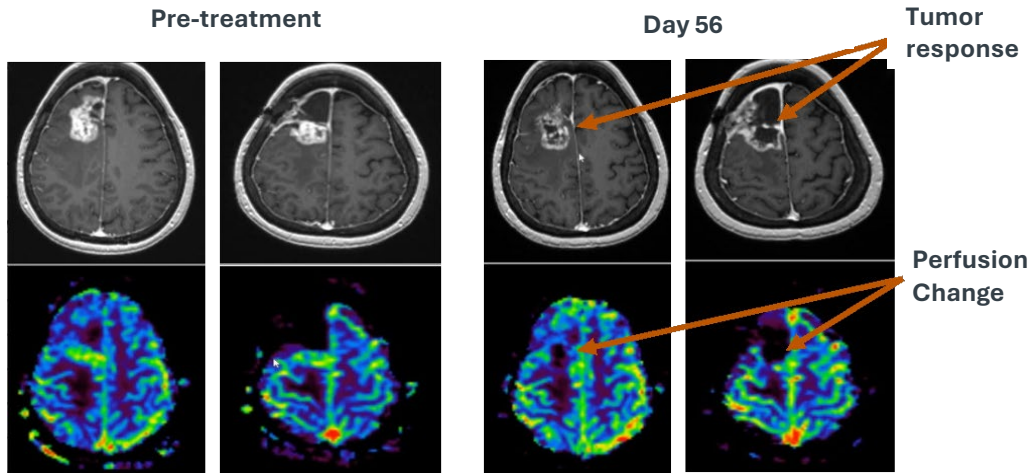
- + OS increased by **27%** for each **10% increase** in the **percentage of tumor covered** ( $p < 0.001$ )<sup>1</sup>
- + OS increased by **31%** for each **100 Gy increase** in the **absorbed dose** ( $p < 0.001$ )<sup>1</sup>

1. Cox Proportional Hazards Model after adjustment for age, baseline ECOG status, baseline volume administered, and baseline tumor volume at time of analysis, November 2023

# ReSPECT-GBM Phase 1 Single Administration Dose Escalation Trial

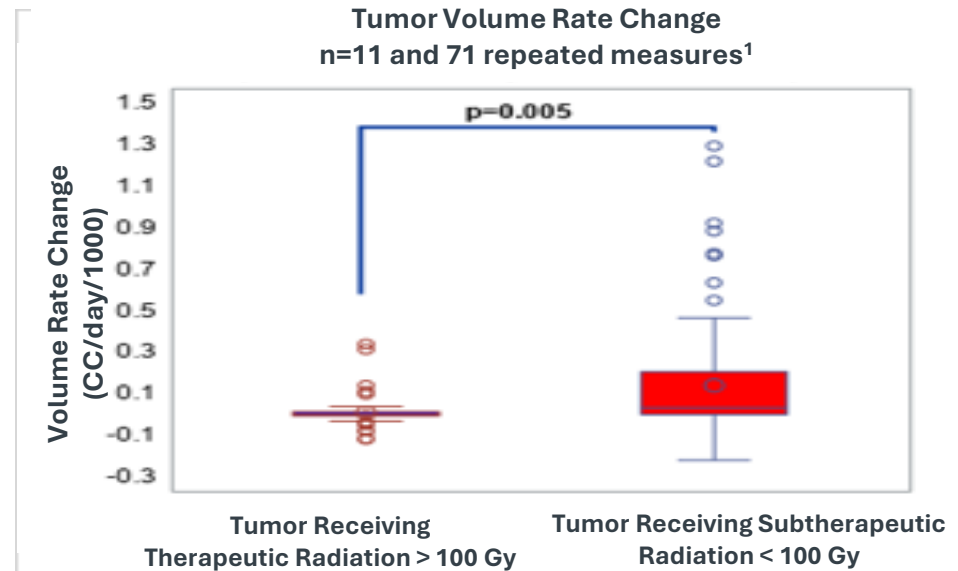
Differentiation of tumor response, progression or pseudoprogression after  $^{186}\text{RnL}$  treatment

## Qualitative Response via Relative Cerebral Blood Flow rCBV Analysis



- + Quantifying treatment response after radiation is challenging
- + MRI with perfusion show qualitative tumor volume changes, indicating response

## Quantitative Response of Treated vs. Untreated Tumor 'Flipbooks' Analysis

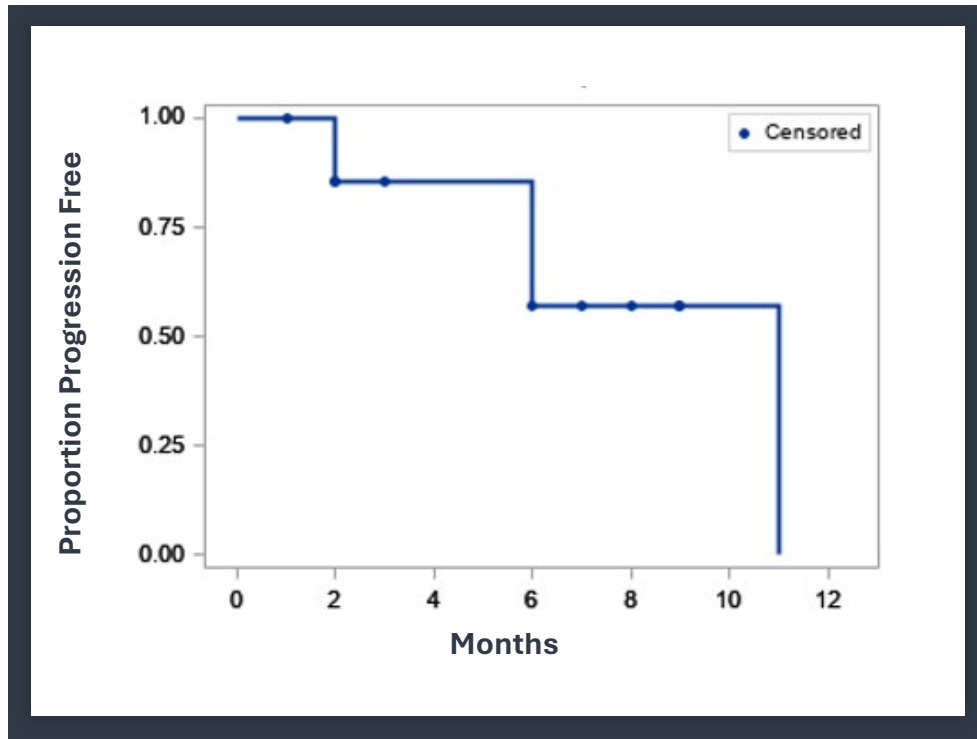


- + Volumetric assessment of response within tumor based on key delivery parameters such as absorbed dose
- + Tumor control (response) occurs in areas receiving 100 Gy or greater

# ReSPECT-GBM Phase 2 Single Administration Dose Escalation Trial

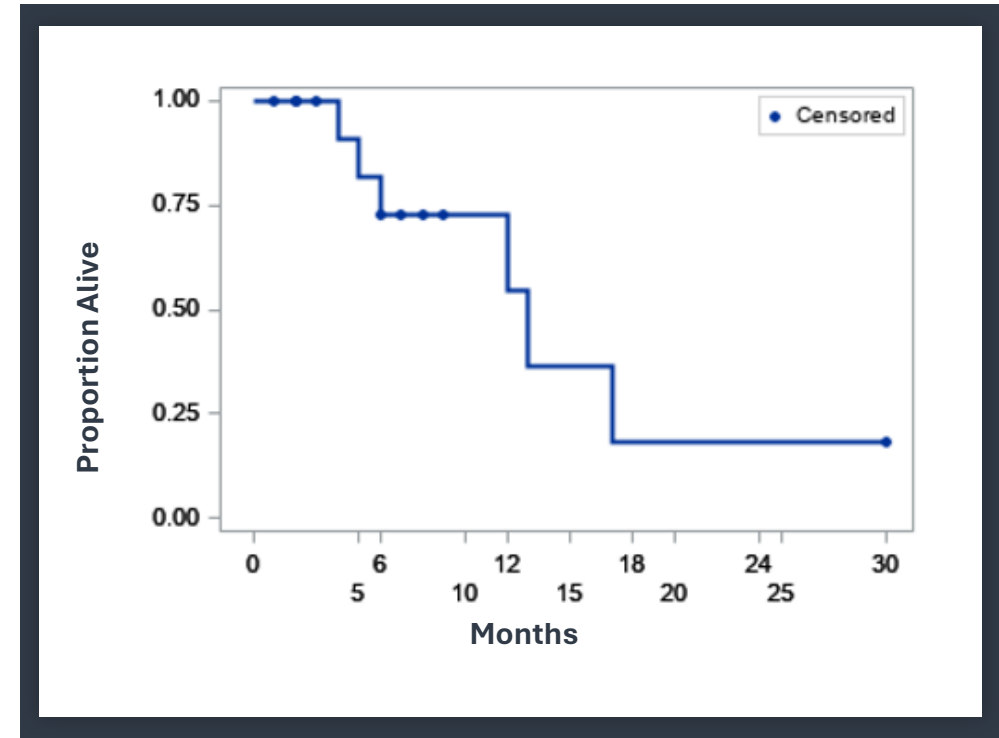
Interim data in P2 trial<sup>1</sup> showing favorable progression & survival signal

### Median Progression Free Survival



PFS: 11 months

### Median Overall Survival



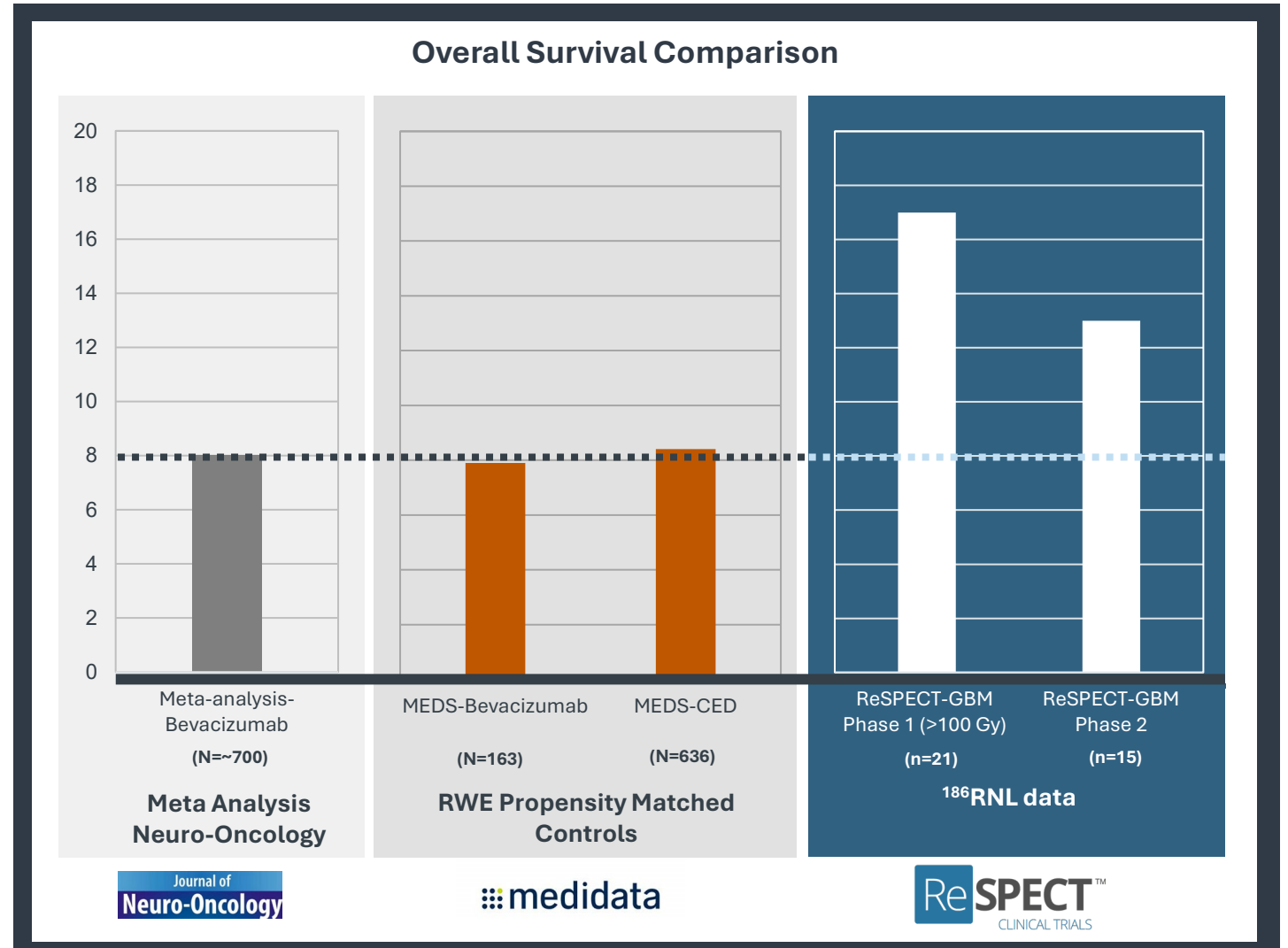
OS: 13 months

1. As of November 2023, n=15

# ReSPECT-GBM Phase 1/2 Single Administration Dose Escalation Trial

Comparability of OS signal observed in the P1/2 trial vs. both published data & RWE

- + Standard of care performance comparison:
  - + Published meta-analysis of >700 rGBM patients
  - + Plus/Medidata conducted 2 propensity matched RWE control arms to Plus Phase 1 data
- + ReSPECT-GBM Phase 1 Trial:
  - + All patients: 38% improvement over RWE control (through RP2D)
  - + 113% improvement over RWE control in patients receiving therapeutic dose radiation (>100Gy)
- + ReSPECT-GBM Phase 2 Trial:
  - + 63% improvement (n = 15 of 34 planned patients<sup>1</sup>)



1. As of November 2023

Note: Data sourced from the Medidata Enterprise Data Store (MEDS) of deidentified patient-level historical clinical trial data, study and patient-level data from historical rGBM CED studies [D'Amico, J Neurooncol 2021], and from ongoing ReSPECT-GBM study.

Note: Intertrial comparison; Intertrial comparisons may be affected by differences in trial conditions and patient characteristics.



# Solid CNS Malignancies

## + Summary

- + Reliable delivery to the tumor/ROI of up to 10-20x radiation vs. EBRT
- + High therapeutic index with minimal systemic toxicity
- + Derived RP2D of 22.3 in 8.8 mL for patients with tumor volumes of 20 mL or less
- + Continue dose escalation in Phase 1 and MTD not reached
- + Tumor imaging response data highly correlates with absorbed radiation dose and mOS
- + Promising mOS signal in both Phase 1 and ongoing Phase 2 trial
- + Development contract with Brainlab to develop next generation CED planning technology
- + Potential new paradigm for delivery of radiation for solid CNS malignancies

## + Next Steps and Expected Milestones

### + **ReSPECT-GBM**

- + Complete enrollment in Phase 2 by mid-2025

### + **ReSPECT-PBC (pediatric brain cancer)**

- + IND accepted and initiate enrollment of Phase 1 for pediatric & ependymoma and high-grade glioma patients in 2025



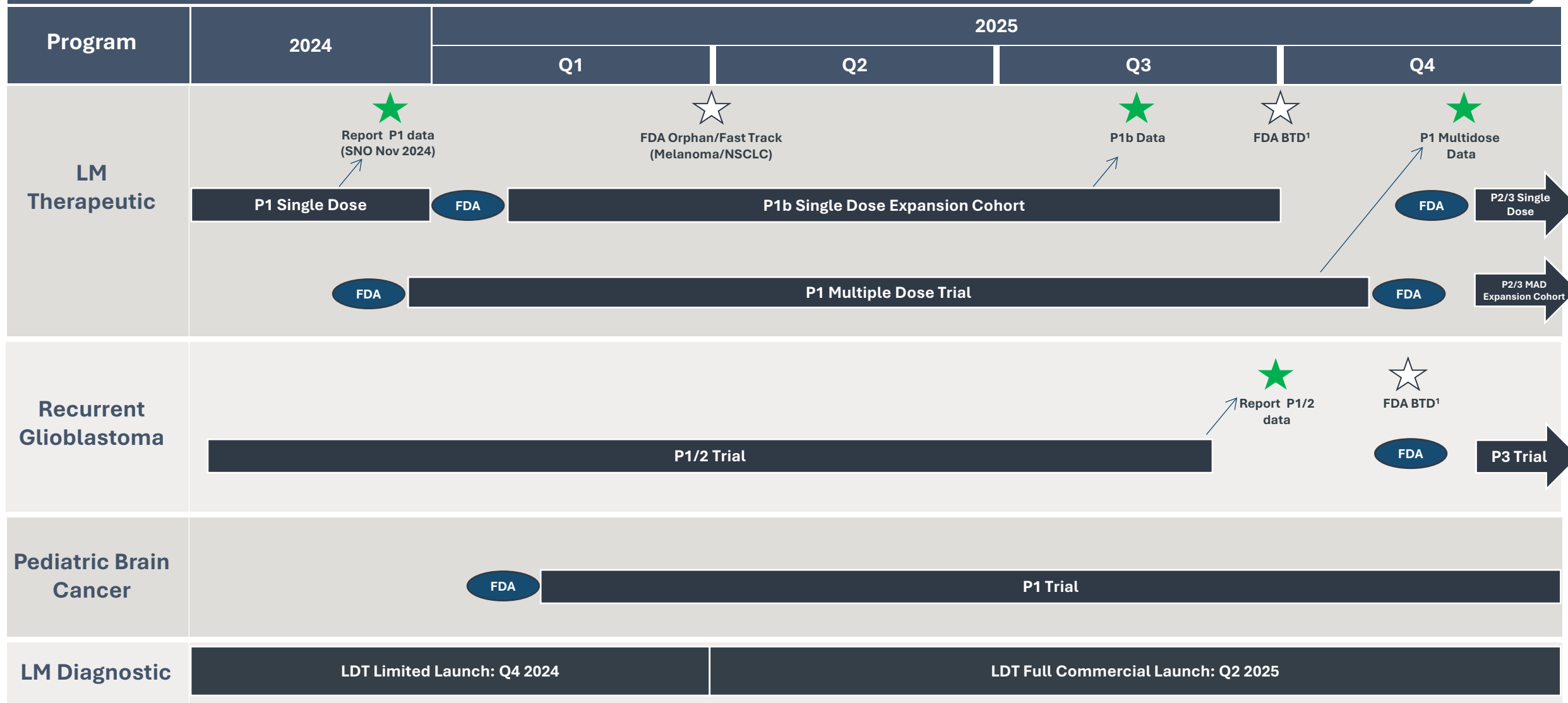
# Financials and Milestones

**Power and precision** in  
cancer radiotherapeutics



# Upcoming Catalysts and Cash Runway

Current cash runway & grant proceeds expected to provide cash through 2025



FDA meeting  
 FDA Designation  
 Data read out  
 Beyond 2025

1. Breakthrough therapy designation

# Plus Therapeutics: Investment Highlights

Differentiated clinical stage targeted radiotherapeutics company

- + Clinical stage radiotherapeutics company focused on CNS cancers
- + Rhenium ( $^{186}\text{Re}$ ) represents a differentiated therapeutic radionuclide with favorable attributes for CNS (many cancers)
- + Incorporates clinically-proven drug delivery modalities
- + Nanoliposome-encapsulated radiotherapeutics achieved very high therapeutic index
- + Mature supply chain and straightforward last-mile logistics
- + Developing both first-in-class therapeutic and diagnostic/biomarker for leptomeningeal disease



# THANK YOU!

For Our Latest News and Updates:

 [@PlusTherapeutics](#)

 [@PlusTherapeutics](#)

 [@PlusTxInc](#)

 [@PlusTherapeutics](#)

 [@PlusTherapeutics](#)

 PSTV





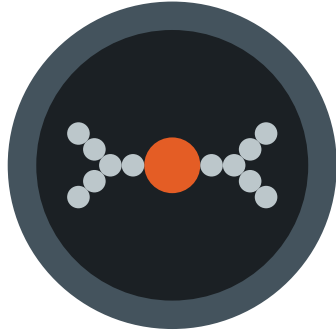
**Power and precision**  
in cancer radiotherapeutics

# APPENDIX



# Plus' Secondary and Preclinical Pipeline

3 areas of ongoing development for pipeline expansion



**$^{186}\text{RNL}$**

Indication expansion

- + Primary GBM
- + Brain metastases
- + Malignant Ascites and Effusions
- + Head and Neck Cancers



**Rhenium Biodegradable  
Alginate Microspheres**

Next Generation Selective  
Internal Radiotherapy

- + GBM
- + Liver cancer
- + Other solid tumors



**CNSide™ Diagnostic/Biomarker**

Cerebrospinal Fluid Circulating  
Tumor Cell Diagnostic

- + CTC + FISH + NGS
- + Diagnosis of LM
- + LM disease monitoring

# CNSide™ CSF Assay Acquisition

Strategic and Synergistic Opportunity for Near-Term Growth

**CNSide™ is a testing platform for CSF tumor diagnosis, treatment/disease monitoring and detection of actionable biomarkers**



**Initial acquisition rationale - expands LM therapeutic TAM for <sup>186</sup>RNL by 2-4x**

- + Acquired all IP and assets
- + Doubles LM diagnostic sensitivity vs. cytology: CNSide™ (80%) vs. cytology (29%)
- + CTC for LM diagnosis and disease monitoring testing implemented in Feb 2024



**Attractive standalone and near-term partnering opportunity**

- + Milestones achieved since licensing/acquisition:
  - + Assets placed in wholly owned sub: CNSide™ Diagnostics LLC
  - + Expanded IP portfolio
  - + Analyzed and reported positive clinical utility data 'FORESEE' (exceeded primary / secondary EPs)
  - + Obtained CLIA registration as an LDT
  - + Included in NCCN guidelines with planned expansion
  - + Applied for reimbursement code with AMA
  - + >10 publications- published, in press, submitted validating clinical utility



# Clinical Development Strategy: Neuro-oncology Steering Committee

## Multi specialty thought leader advisory panel

- + **Andrew Brenner, MD, PhD:** Professor-Research, Departments of Medicine, Neurology, and Neurosurgery; Clinical Investigator, Institute for Drug Development; Co-Leader, Experimental and Developmental Therapeutics Program; S and B Kolitz/CTRC-Zachry Endowed Chair Neuro-Oncology Research Mays Cancer Center at UT Health San Antonio
- + **Priya Kumthekar, MD:** Associate Professor, Neurology; Northwestern Feinberg School of Medicine, Director of the Brain Metastasis Program of the Robert H. Lurie Comprehensive Cancer Center
- + **Jonathan Yang, MD, PhD:** Member of the Faculty, Department of Radiation Oncology at NYU Grossman School of Medicine; Associate Vice Chair, Clinical Research and Developmental Therapeutics, Department of Radiation Oncology; Director, Clinical Research, Brain Spine Tumor Center, Laura and Isaac Perlmutter Cancer Center
- + **Seema Nagpal, MD:** Clinical Professor, Neurology and Neurological Sciences; Clinical Professor, Neurosurgery, Stanford University
- + **Stuart Grossman, MD:** Co-Director, Brain Cancer Research Program, Sidney Kimmel Cancer Center, Johns Hopkins Medicine
- + **Elcin Zan, MD:** Chair, Division of Nuclear Medicine, Cleveland Clinic



Dr. Nagpal



Dr. Kumthekar



Dr. Yang



Dr. Grossman



Dr. Brenner



Dr. Zan

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