



## Corporate Update

January 2026

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Power and precision  
in cancer radiotherapeutics

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,” “planning”, “projecting”, “expecting” 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 REYOBIQ™ including the ability of REYOBIQ™ 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 CNSide, REYOBIQ™ 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 REYOBIQ™; the continued evaluation of REYOBIQ™, 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, including the ability to come into compliance with The Nasdaq Capital Market listing requirements; 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 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, 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](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.

# Executive Summary

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**PLUS**<sup>®</sup>  
THERAPEUTICS

**Re**SPECT  
CLINICAL TRIALS

 **REYOBIG**<sup>™</sup>  
rhenium re 186  
obisbameda injection

**CNSide**<sup>™</sup>

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# Plus Therapeutics (PSTV) Overview

## Best-In-Class Diagnostic for CNS Mets - CNSide®: >\$6B TAM

- + U.S. commercial relaunch Q3 2025 – Projected 500K patients / year
- + Announced first of planned national coverage agreements, with UnitedHealthcare and Humana
- + Previously commercialized, ordered by 120 U.S. institutions
- + Data and analytics for personalized therapeutic approach and predictive models



## First-In-Class Radiotherapeutic for CNS Cancers: >\$16B TAM

- + Safe, precision therapy with up to 20x radiation delivery vs. standard of care
- + FDA Fast Track & Orphan Designations facilitate expeditious approval process



## Multiple Mid-Stage ReSPECT Clinical Trials of REYOBIQ™

- + First-in-class drug treating leptomeningeal mets (LM), Dosing/Phase 2 trial enrolling
- + Completing recurrent glioblastoma (rGBM) Phase 2 trial in 2025



Glossary:

rGBM – recurrent glioblastoma

LM – leptomeningeal metastases

PBC – pediatric brain cancer

Tx – radiotherapeutics CNS – central nervous system

Dx – diagnostic

mets – metastases

mOS – median overall survival

SOC – standard of care

TAM – total addressable market

BBB – blood brain barrier

MTD – maximum tolerated dose

CTC – circulating tumor cells

CSF – cerebral spinal fluid

# Company Overview

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**PLUS**<sup>®</sup>  
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**Re**SPECT  
CLINICAL TRIALS

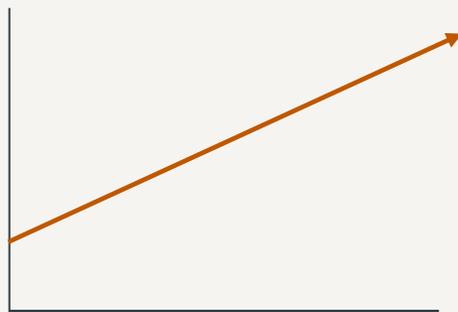
 **REYOBIQ**<sup>™</sup>  
rhenium re 186  
obisbameda injection

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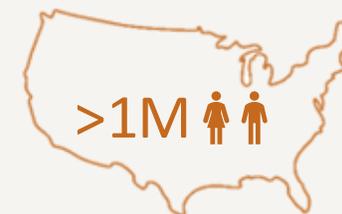
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# Epidemic of Central Nervous System Cancers

*Growing mets epidemic dwarfs incidence of primary brain cancers 10:1 ratio*



Epidemic due to improved outcomes for primary cancer treatments (breast, lung, melanoma, etc.)



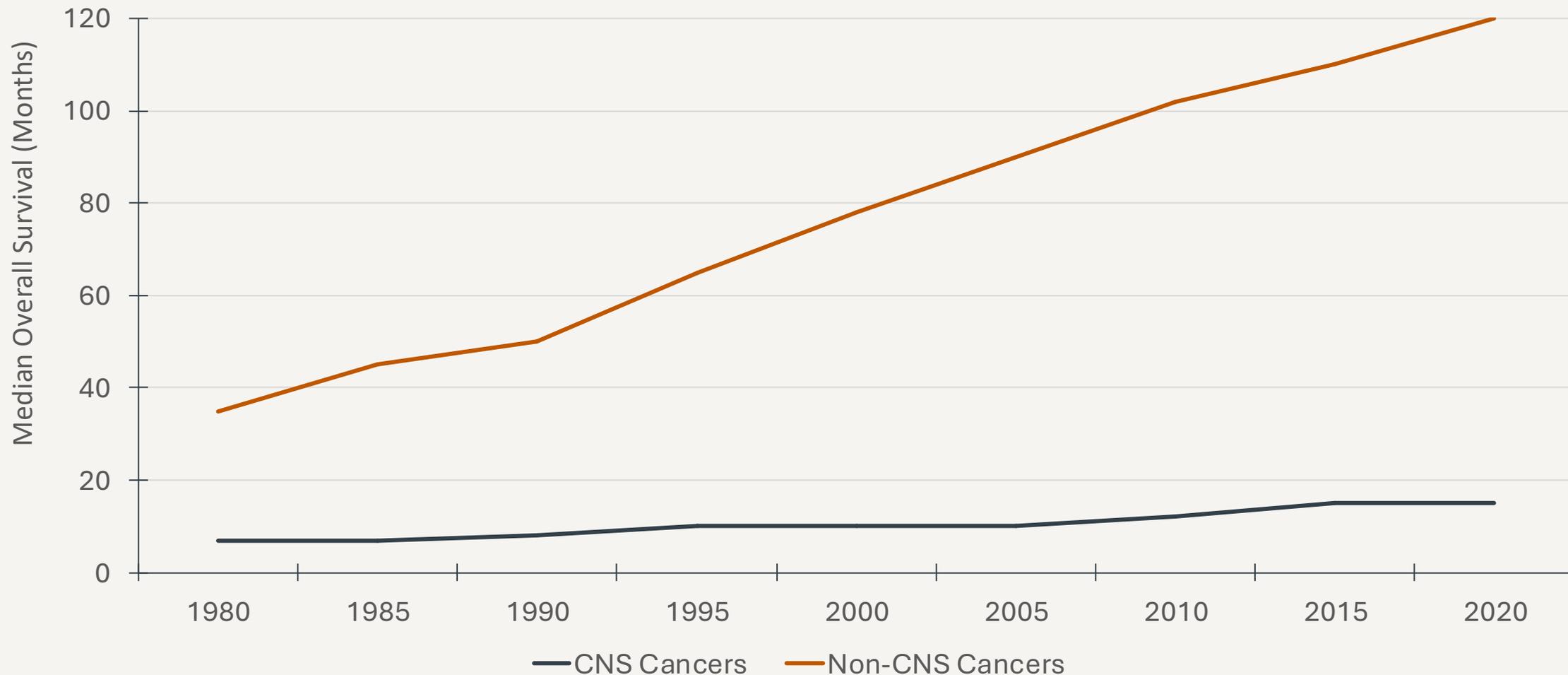
Over 1 million patients at risk of CNS mets in U.S.<sup>1</sup>



Up to 30% of adult cancer patients will develop CNS mets<sup>1</sup>

# CNS Cancer Survival Rate- Little Progress Over 40 Years

*The 4 decade-old CNS cancer 'playbook' has not worked*



# Limitations to Gains in CNS Cancer Survival

*The unique nature of the CNS creates both diagnostic & therapeutic challenges*



## Poor Diagnostic Options

Leptomeningeal Mets: 2-4x underdiagnosed<sup>1</sup>  
Standard diagnostic Cytology from 1904<sup>2</sup>  
Better imaging has not been the answer



## Surgery

If operative, clean tumor margins unobtainable



## External Radiation

Proven MOA,  
dosing limited



## Pharmaceuticals

Only 2% of drugs can cross BBB  
Genetic drift common in mets

# Roadmap to Improve CNS Cancer Survival

*Plus is creating a new playbook*

- ✓ **Improved Diagnostic** – CNSide Dx Platform
  - **Better Biomarkers / Concrete Outcomes Measures** – CSF circulating tumor cells
- ✓ **Improved Therapeutic** – REYOBILQ targeted radiotherapeutic
  - **Reduce / Remove Impact of the BBB** - Innovative Drug Delivery
- ✓ **Unified Advanced Data Analytics** – Dx & Tx Improvements + Partnerships

# Plus' Playbook to Improve Survival in CNS Cancers

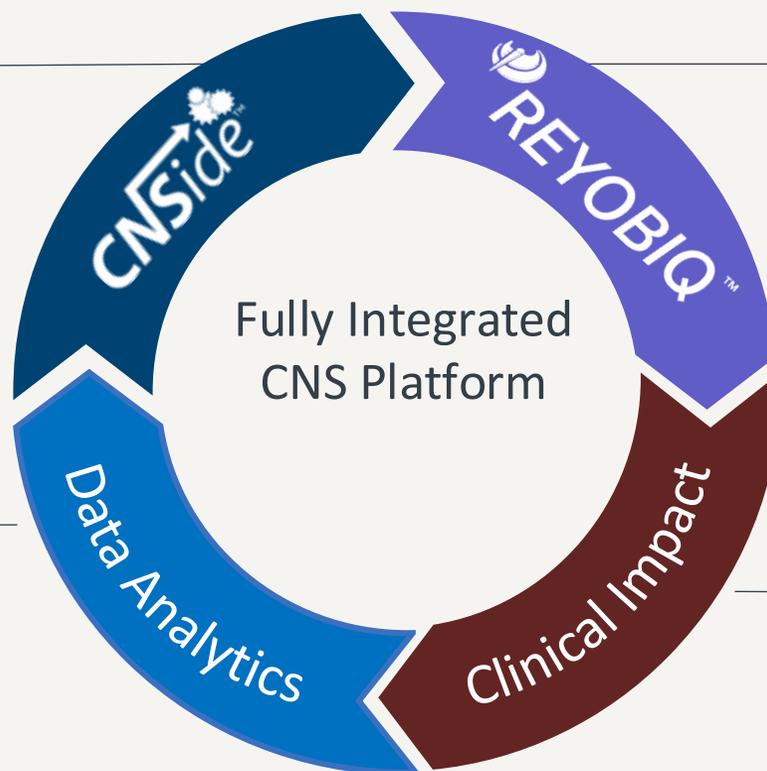
Focused 'Roche' model for CNS oncology

## CNSide Diagnostics

- + Launched in late 2025
- + Nearing 100m covered lives
- + \$6B opportunity\*

## Unified data analytics platform

- + CNSide cellular and molecular data
- + REYOBIQ imaging & delivery data
- + Pipeline development
- + Further OS gains



## Lead drug REYOBIQ

- + Up to 20x radiation delivery
- + Bypass BBB
- + No MTD reached in multiple clinicals
- + \$16B opportunity\*

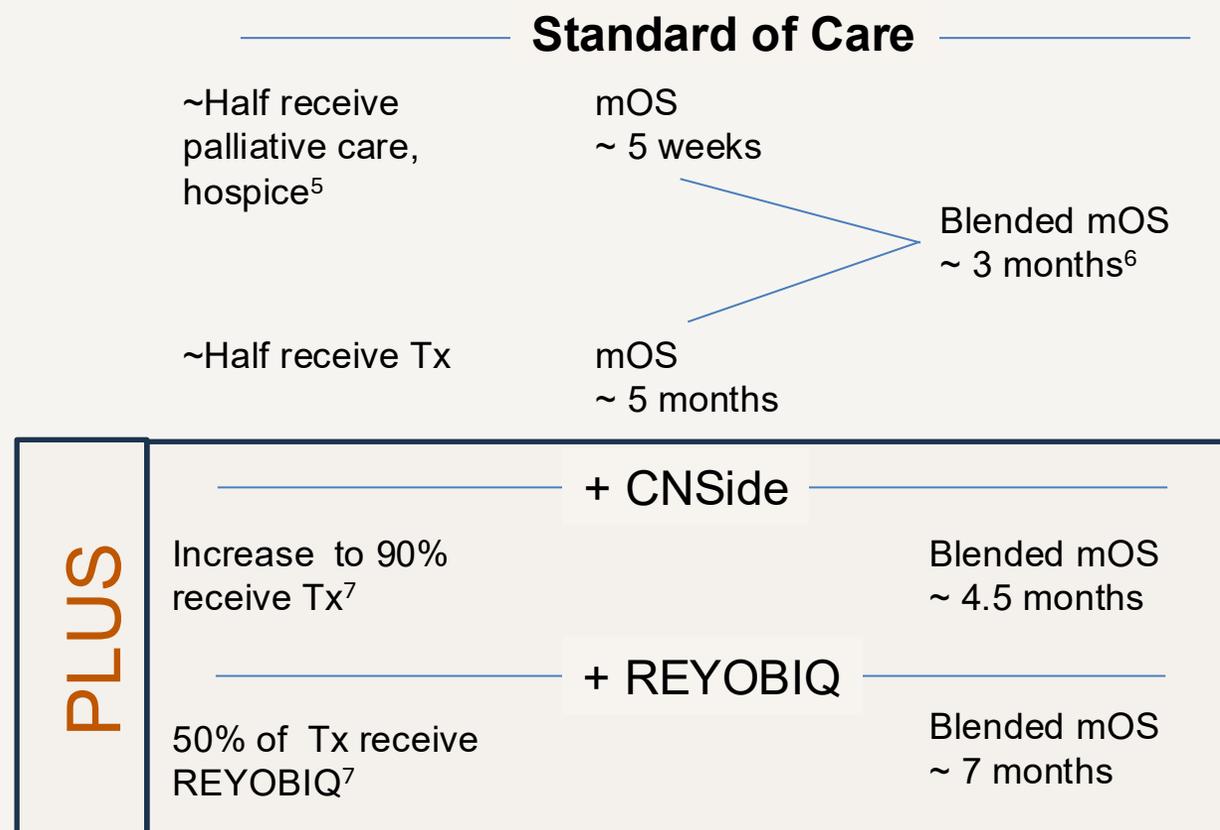
## Improved survivals in LM

- + CNSide: est. 50% inc. in OS
- + REYOBIQ: est. additional 50% inc. in OS

# LM Epidemiology & Standard Care Pathway

Near term path to doubling survival in LM

- + US LM Diagnoses ~ 125,000/year<sup>1</sup>
- + Underdiagnosed: LM cases are 2-4x more common based on autopsy findings<sup>2</sup>
- + Poor survival: 4-6 weeks without treatment vs. 4-6 months with treatment<sup>3</sup>
- + Primary Solid Cancers: ~ 80% of cases due to breast & lung CA and Melanoma<sup>4</sup>



1. Nayar G, et al. Leptomeningeal disease: current diagnostic and therapeutic strategies. *Nature Reviews Clinical Oncology*. 2017;DOI: 10.1038/nrdclinonc.2017.128
2. Le Rhun E, et al. – Leptomeningeal metastasis: a RANO proposal *Lancet Oncology*, 2017
3. Boire A. Metastasis to the Central Nervous System. *Continuum (Minneapolis)*. 2020 Dec;26(6):1584-1601. doi: 10.1212/CON.0000000000000939. PMID: 33273173; PMCID: PMC9924436
4. *J Exp Med* (2024) 221 (4): e20212121. <https://doi.org/10.1084/jem.20212121>
5. Gensler, R., Xia, Y., Horowitz, M.A. et al. Outcomes of leptomeningeal disease after only vertebral osseous metastases: a real-world analysis using the TriNetX database. *J Neurooncol* 175, 219–229 (2025). <https://doi.org/10.1007/s11060-025-05122-w>
6. Batoal A, Kasi A. Leptomeningeal Carcinomatosis. [Updated 2023 Mar 27]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK499862/?referre=grok.com>
7. Management estimates

# TAM for CNSide & REYOBIQ in CNS Mets

*Initial focus on Leptomeningeal Mets with significant growth potential in Brain Mets*

## 500K+

Total CNS Mets Patients\* 1,2,3,4,5

## \$6B+

U.S. Total Addressable Market\*

## 56,250

REYOBIQ Patients\*

## \$16B+

U.S. Total Addressable Market\*

\*Notes:

- 500K+ CNS mets patients include incidence, at risk, and prevalence populations (base case estimate)
- \$6B TAM assumes 4.3 tests/patient at ~\$3,000 list price (base case estimate on # of tests and pricing)
- \$16B TAM assumes 56,250 (50% of 90% of the current US LM diagnoses) LM patients receiving 3 REYOBIQ doses @ \$100,000 per dose

1. Cagney, D.N., et al. Neuro Oncol 19(11), 1511–1521 (2017). <https://doi.org/10.1093/neuonc/nox077>
2. Groves, M.D. Neurosurg Clin N Am 22, 67–78 (2011). <https://doi.org/10.1016/j.ne.c.2010.08.006>
3. Lamba, N., et al. Neuro Oncol 23(9), 1447–1456 (2021). <https://doi.org/10.1093/neuonc/noab101>
4. Le Rhun, E., et al. Surg Neurol Int 4, 265 (2013). <https://doi.org/10.4103/2152-7806.111304>
5. Nguyen, A., et al. Curr Oncol 30(6), 5906–5931 (2023). <https://doi.org/10.3390/currncol30060442>

## 2026 Milestones

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### Diagnostic

- + Reach > 150 million covered lives for CNSide Diagnostic platform
- + Obtain Medicare and Medicaid coverage
- + Establish prior commercial order rate (1,250 TCE tests per annum)
- + Establish 50 or more unique ordering physician customer base for CNSide
- + Expand platform and launch additional CSF tumor characterization tests

### Therapeutic

- + Complete enrollment in ReSPECT-GBM Phase 2 trial for recurrent glioblastoma and conduct end of phase meeting to align on pivotal trial design
- + Define optimal dose/interval for REYOBIQ in ReSPECT-LM Phase 2 expansion trial and begin enrollment
- + Complete manufacturing scale-up for REYOBIQ commercial and approval trial supply
- + Enroll first patient in the ReSPECT-PBC pediatric brain cancer Phase 1 trial with REYOBIQ

\* These statements and figures are targets for 2026 and are not projections and should not be relied upon as such. Further, these targets are subject to occurrences that may negatively impact our business and our industry generally, which may be out of our control, and which may impact our ability to achieve these targets.

# Executive Management Team

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Marc H. Hedrick, MD MBA  
President & CEO, Plus Therapeutics

30+ years of clinical development and business leadership



Russ Havranek, MS MBA  
Executive VP Corporate Strategy &  
Business Development

25+ years of development &  
commercialization experience



Andrew Brenner, MD PhD  
Interim CMO  
Professor of Medicine and  
Neuro-Oncology  
Clinical Investigator  
Endowed Chair, Mays Cancer  
Center, UT Health San Antonio



Russell Bradley  
President & General Manager  
(CNSide)

30+ years of diagnostic & life  
sciences leadership



Andrew Sims, CPA  
CFO & VP of Finance

25+ years of Financial  
Leadership

# Diagnositics

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## Poor Diagnosis Standards in CNS Mets

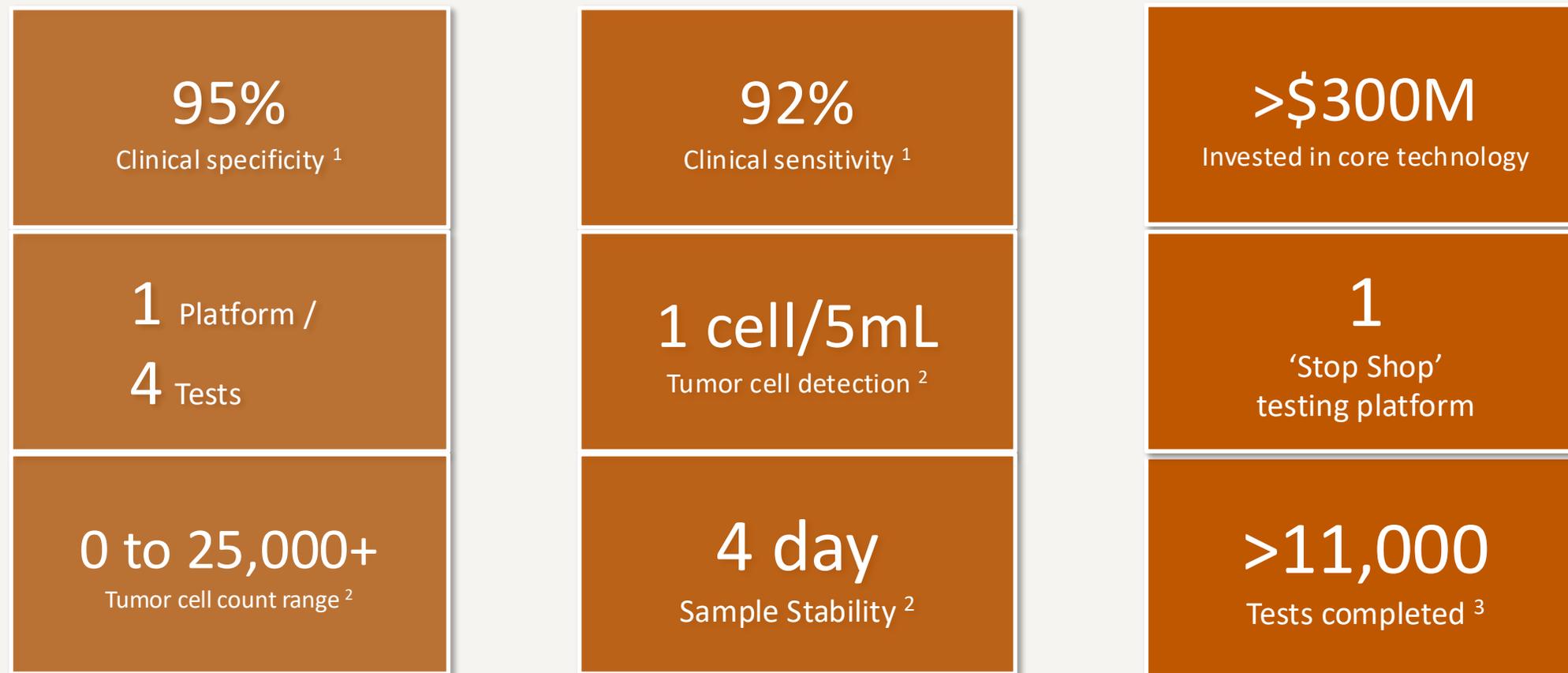
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The current standard for LM diagnosis (cytology) introduced in **1904**<sup>1</sup>

- + Cytology: not quantitative, ~ 50% sensitive, no FDA support an as endpoint<sup>2</sup>
- + Imaging: not quantitative, ~75% specific, no FDA support an as endpoint<sup>2</sup>
- + Neither tool helps disease monitoring or treatment selection
- + Therefore 'therapeutic nihilism' is common and hospice referrals high

# A Comprehensive CNS Diagnostic Solution

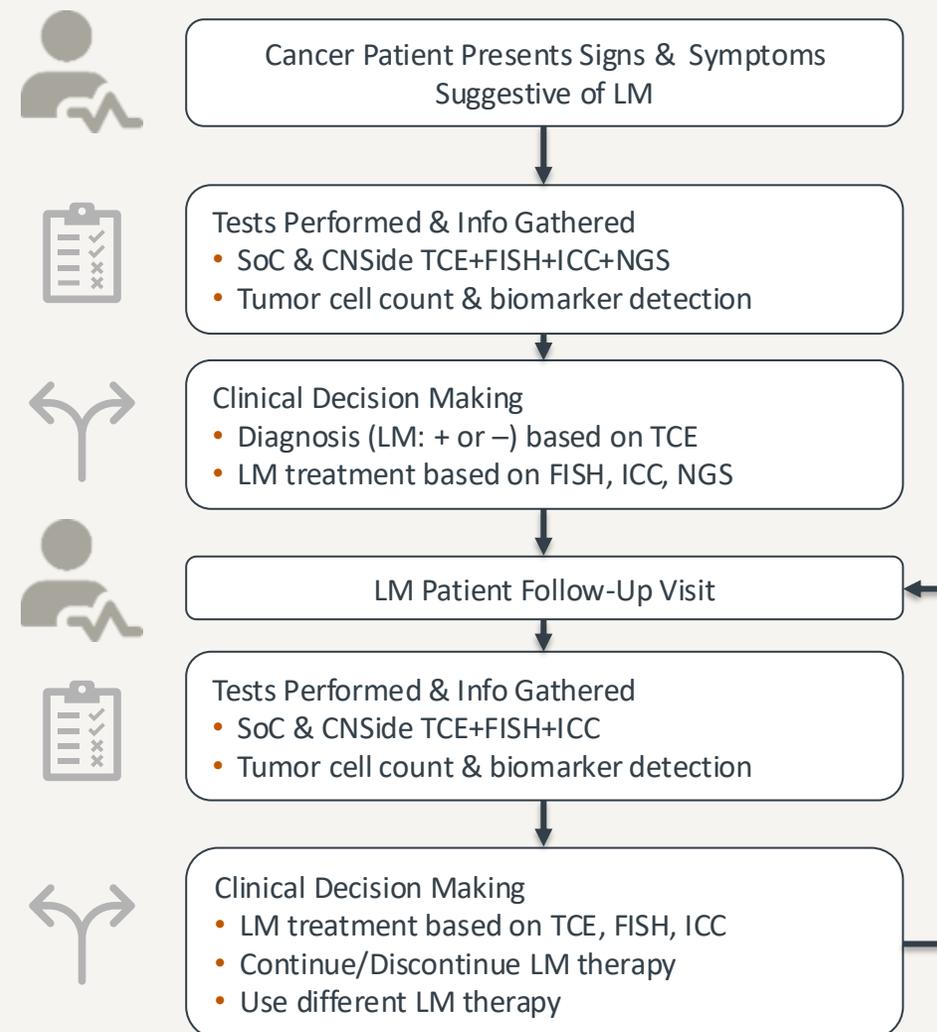
*Proprietary & highly sensitive tumor cell capture & interrogation system optimized for CNS mets*



1. Sweed, N., et al. Arch Pathol Lab Med (2025) 149 (3): 242–252. <https://doi.org/10.5858/arpa.2023-0295-OA>  
 2. Management estimates  
 3. Historical Commercial Data

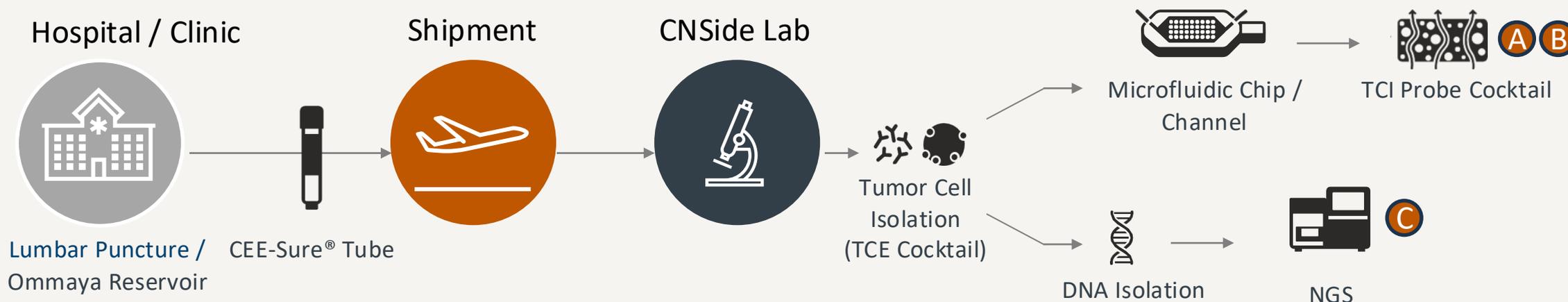
# Platform with 4 Tests from a Single Sample

- 1** CNSide® CSF Tumor Cell Enumeration (TCE)  
 Detects LM tumor cells in CSF; quantifies LM tumor cells for diagnosis & treatment monitoring
- 2** CNSide® CSF Fluorescence In Situ Hybridization (FISH)  
 Identifies gene expression abnormalities using fluorescent probes; used by physicians to personalize therapy selection
- 3** CNSide® CSF Immunocytochemistry (ICC)  
 Confirms origin of tumor cells & identifies gene expression abnormalities
- 4** CNSide® CSF Next-Generation Sequencing (NGS)  
 Detects clinically relevant mutations in DNA & RNA



# CNSide Dx Platform: Products & Services

*Provides a unique & clinically actionable dataset for providers*



## Proprietary Tech Manufactured In-house (Product):

1. CEE-Sure Tube
  - Preserves collected CSF specimen (LP/OR)
2. Microfluidic Chip
  - Cell capture for tumor cell enumeration
3. Cell Interrogation Probe Cocktail
  - Cell capture for tumor cell interrogation

## Data Reports w/ Pathologist Interpretation (Service):

- A. Tumor Cell Enumeration (TCE)
  - Quantifies tumor cell count
- B. Tumor Cell Interrogation (TCI)
  - Identifies gene expression / guides treatment
- C. Cell Free DNA Analytics (CF-DNA)
  - Detected clinically relevant mutations

# A Derisked Commercial Opportunity

*2025 commercial relaunch: clinically proven, market traction, & positioned for scale*

- + Proven high throughput & scalable technology
  - ~\$300M investment in core tech made by original developer
  - 9 peer-reviewed studies and publications
  - Clinically validated (FORESEE trial completed)
  - CSF CTCs in NCCN guidelines\*
  
- + CNSide commercially available since 2020 by original developer (paused 2023)
  - Previously launched & accepted by CMS in 2020
  - 11,000+ tests ordered
  - 200+ unique physician users across 120+ institutions
  - Avg. 4.3 tests/patient
  
- + 1<sup>st</sup> national policy coverages: United Healthcare and Humana
  - 51 million covered lives with United Healthcare
  - 16 million covered lives with Humana



# CNSide Commercial Expansion Plans

*Commercial & operational foundation now in place for growth in 2026 and beyond*

## 2025- Established core commercial & operational capabilities

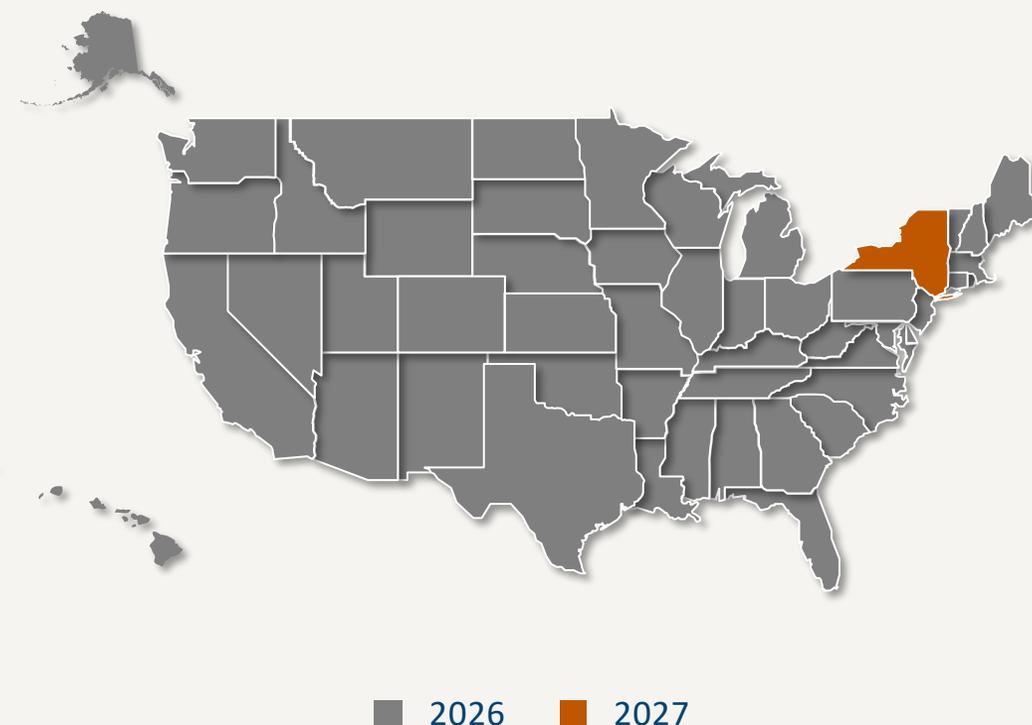
- CLIA certification and broad state licensure
- Commercial operations team and IT infrastructure
- Expand testing operations footprint near Texas Medical Center
- Market access and payor agreements
- Offering via early access program and select academic sites

## 2026- Commercial scale-up phase

- Expand sales team and related functions for national coverage
- Increase covered lives via private & public payor agreements
- Improve test automation and expand product offerings
- Focus on neuro-oncology community

## 2027- Growth phase

- Broaden commercial reach to medical oncologists, private hospitals and clinics
- OUS expansion



# Targeted Radiotherapeutics

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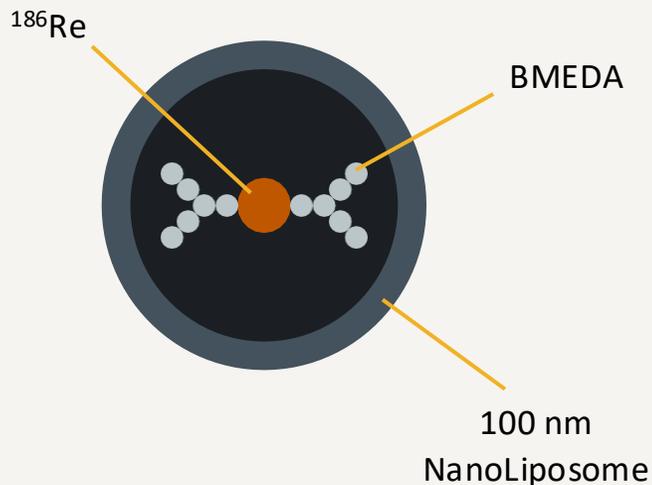
# A First-In-Class Targeted Radiotherapeutic

3 Part Drug Formulation

2 Delivery Modalities

Therapeutic Impact

Radioisotope, Small Molecule, Carrier

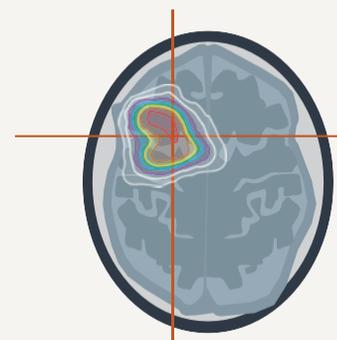


Dual Beta & Gamma Emitter

Intrathecal or Direct-to-Tumor Delivery

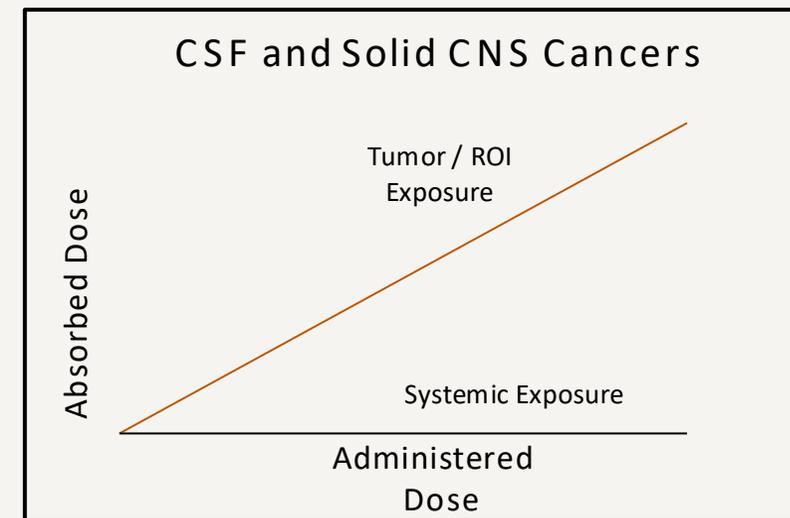


Intraventricular Catheter (Omayo Reservoir)



Convection Enhanced Delivery (CED)

Up to 20x Radiation Dose vs. Standard of Care



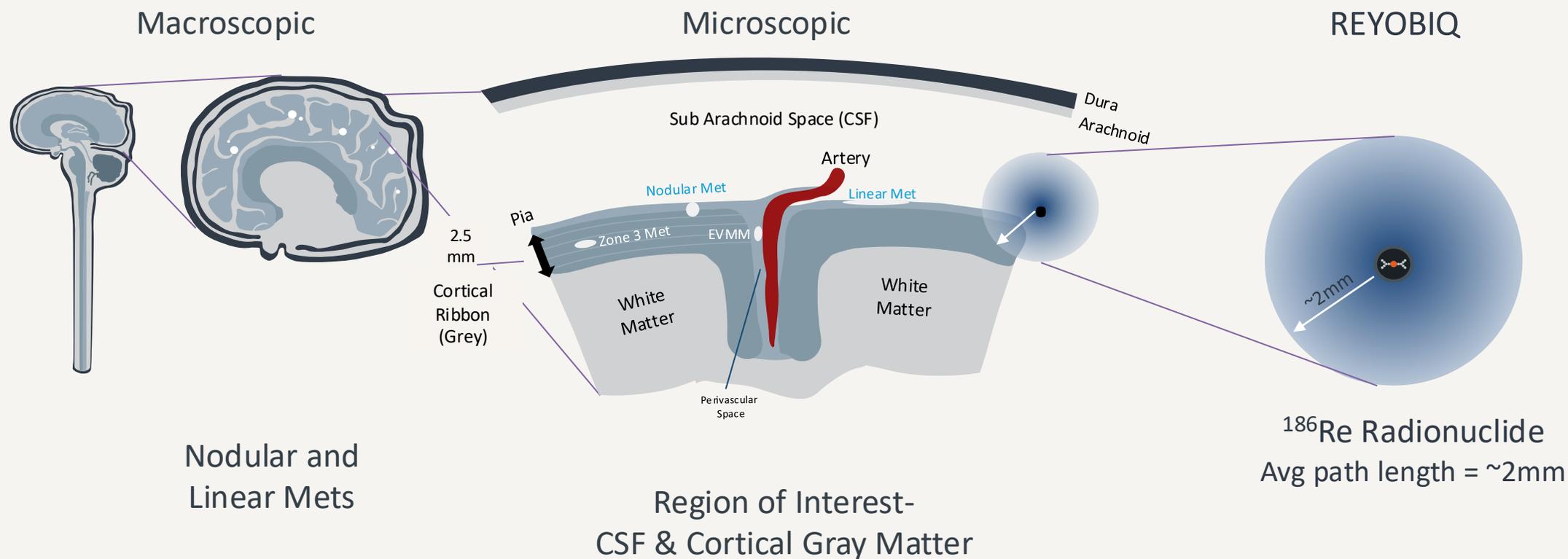
# CNS Radiotherapeutic Pipeline

*Multiple mid-stage trials for unmet medical needs supported by \$25M in grants*

Indication	Trial Design	Phase 1	Phase 2	Phase 3	Projected Milestones
Leptomeningeal Metastases	Single Dose Escalation				Completed
	Dose Optimization				Enrolling, data 2026
Recurrent Glioblastoma	Single Dose Expansion				Enrolling, data 2026
Pediatric Ependymoma & High Grade Glioma	Single Dose Escalation				Enroll 2026

# Pathology of Leptomeningeal Disease and REYOBIQ MOA

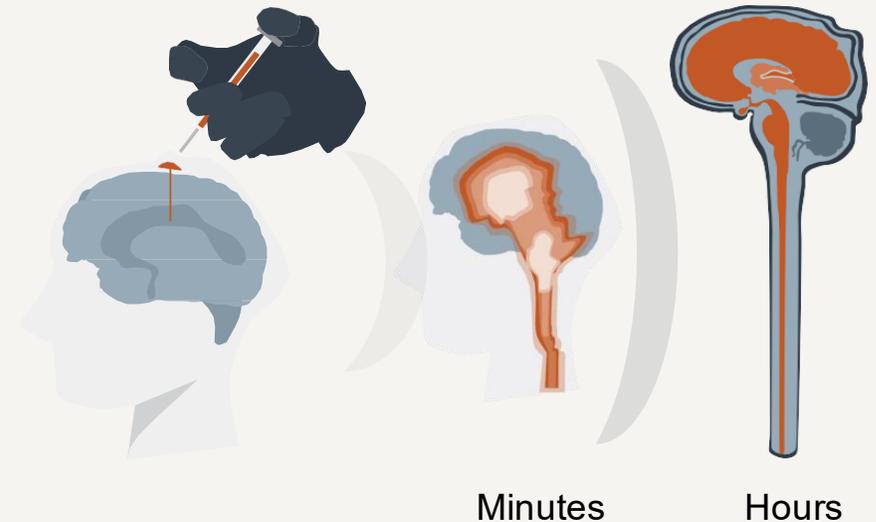
*Rhenium-186 energy profile, delivery modality, path length designed for intrathecal compartmental therapy*



# ReSPECT-LM Phase 1 Single Dose Escalation Trial

*Completed: safe delivery very high doses of radiation, no MTD reached*

- + Single outpatient injection
- + One dose delivers 10x radiation vs 10 doses of fractionated EBRT
- + Dose escalation
  - 6.6 to 75 mCi without max dose reached
  - Recommended Phase 2 Dose (RP2D) 44.1 mCi
- + Safety & Adverse Events (AE)
  - Two most common AEs (<20% of patients) – headache & vomiting
  - Most related AEs either Mild (grade 1, 63%) or Moderate (grade 2, 23%)
  - 4 patients with Serious Adverse Reactions (SARs); 6 total SARs



# LM Phase 1 Single-Dose Escalation Trial Summary Data

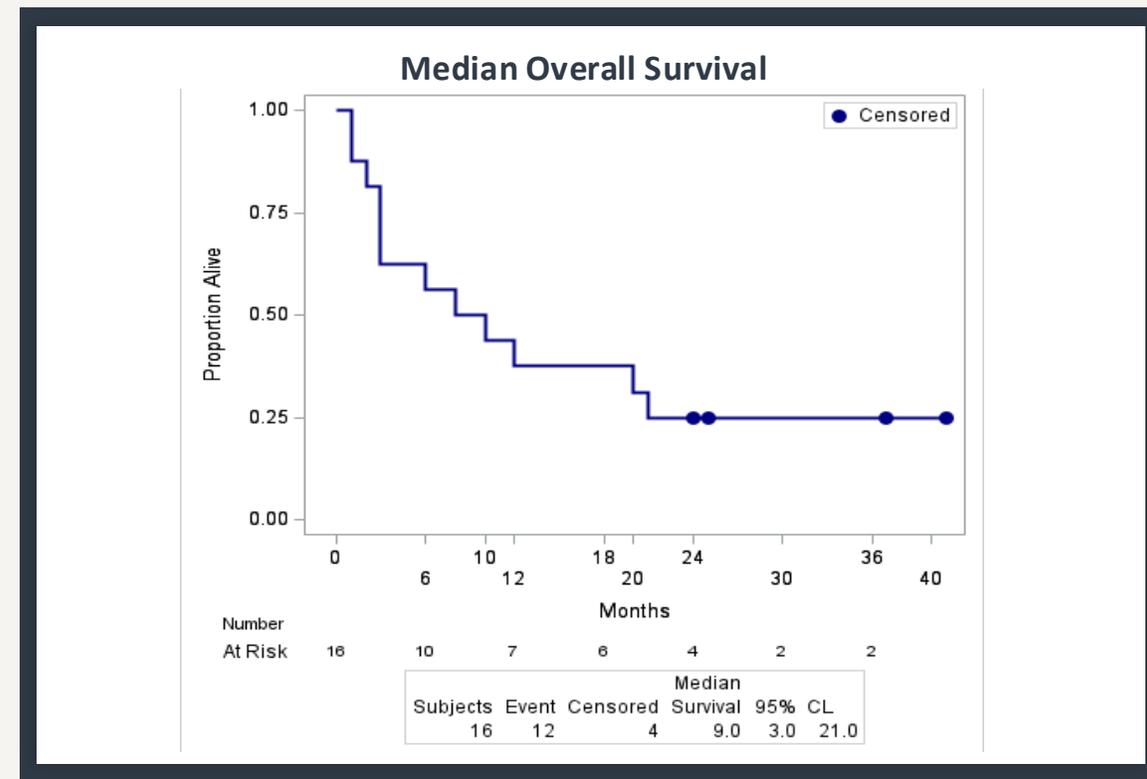
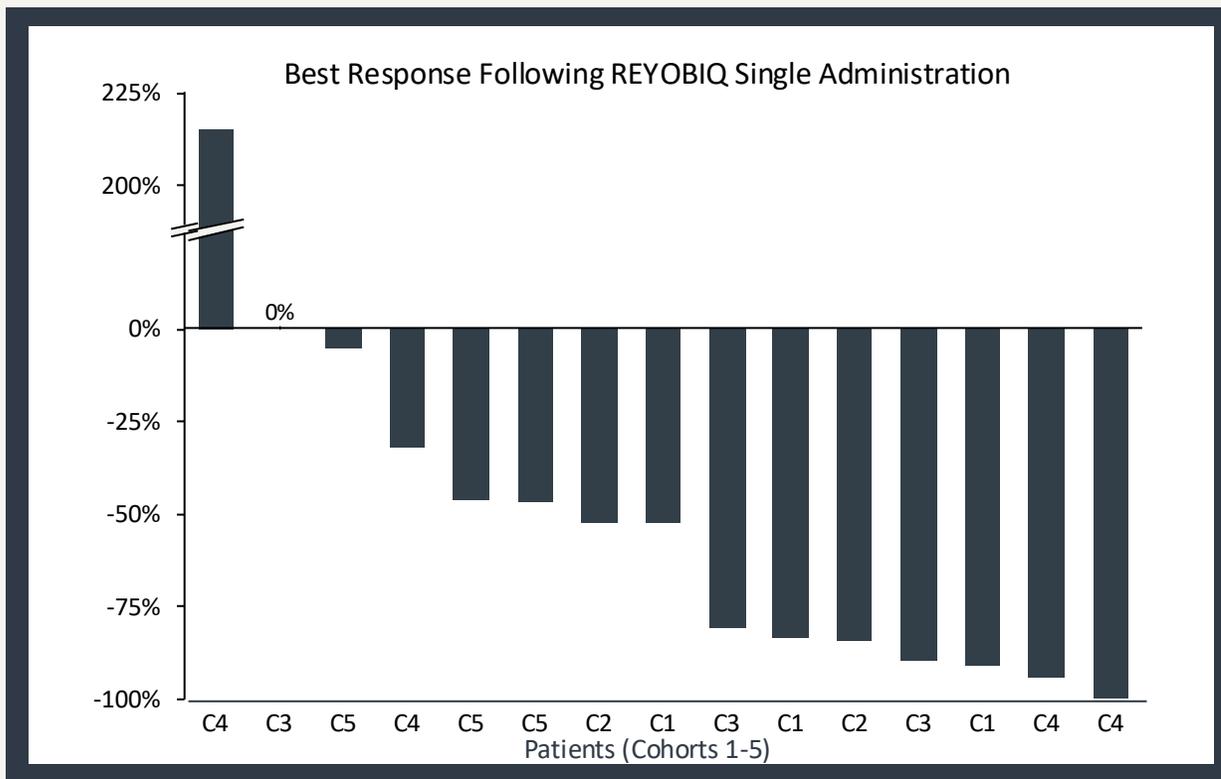
## Comprehensive clinical response across all measures

### Clinical Benefit Rate

- + Circulating tumor cells (CTC) response: 93% (14/15); 5/7 patients w/>80% CTC response survived >1 year
- + MRI imaging response: 76% (13/17)
- + Clinical response: 87% (13/15)

### Median Overall Survival (mOS)

- + mOS of 9 months, compared to 4-6 months reported
- + 4 patients remain alive at analysis<sup>1</sup>



# LM Clinical Development Plan

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*Establishing RP2D and planning for pivotal trial*

## Completed- Phase 1 Single Dose Safety Trial

- + No MTD, MFD of 66 mCi
- + MFD 44.1 mCi
- + Safety & evidence of clinical benefit at 13.2, 26.4 & 44.1 mCi

## Completed FDA End of Phase Meeting NOV 2025

### Enrolling- Multiple Dose Phase 1/2 Trial

- + 3 intervals: every 56, 28 & 15 days (13.2 & 26.4 mCi doses only)
- + 3 doses: 13.2, 26.4 & 44.1 mCi
- + Phase 2 safety/efficacy expansion at 1 or more doses to plan/power pivotal trial
- + Assess improvement in overall survival, patient reported outcomes and neurologic improvement over standard of care

# FDA Meeting and Feedback

*FDA ReSPECT-LM end of phase meeting November 2025*

## **Responses to key sponsor enquiries**

- Accelerated approval- May be appropriate for this indication.
- Primary & key endpoints- FDA stated that there are insufficient data to use CTCs as a surrogate endpoint but provided feedback on additional steps to support validation of CTCs to support future applications. Agency encouraged study of patient reported outcomes, neurologic function as well as overall survival as potential basis of marketing approval. Agency & Sponsor aligned that CTCs could be considered for use as a key secondary endpoint.
- Trial design & comparator group- Agency & Sponsor aligned on a randomized controlled design approach. Agency & sponsor further discussed that the study may include an intrathecal chemotherapeutic as a comparator and approaches to standardize the available comparator chemotherapy regimens as well as any background and rescue interventions under the trial protocol in both active and control arms.
- Treated populations- Agency conveyed that it may be reasonable to incorporate multiple histologies in a single trial, i.e. multiple underlying etiologies in LM.

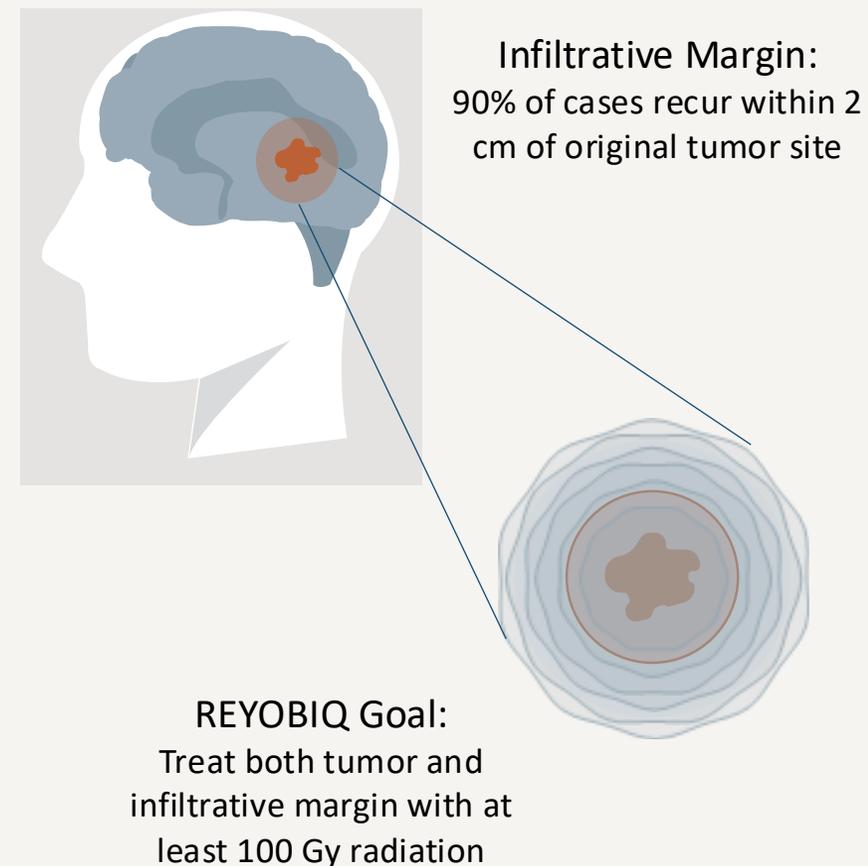
# Recurrent Glioblastoma

*Aggressive & deadly disease, resistant to conventional treatments*

U.S. Annual  
Incidence

15K<sup>1</sup>

- + Most prevalent malignant tumor affecting the brain & CNS<sup>2</sup>
- + Large unmet medical need for GBM patients<sup>2</sup>
  - 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

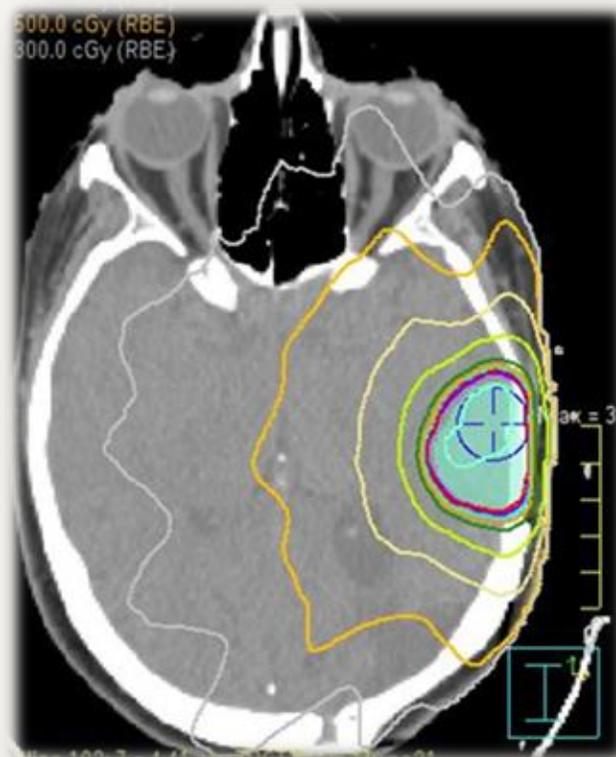


## Advantages vs. External Beam Radiation Therapy

*Better precision & more radiation delivered than gold standard*

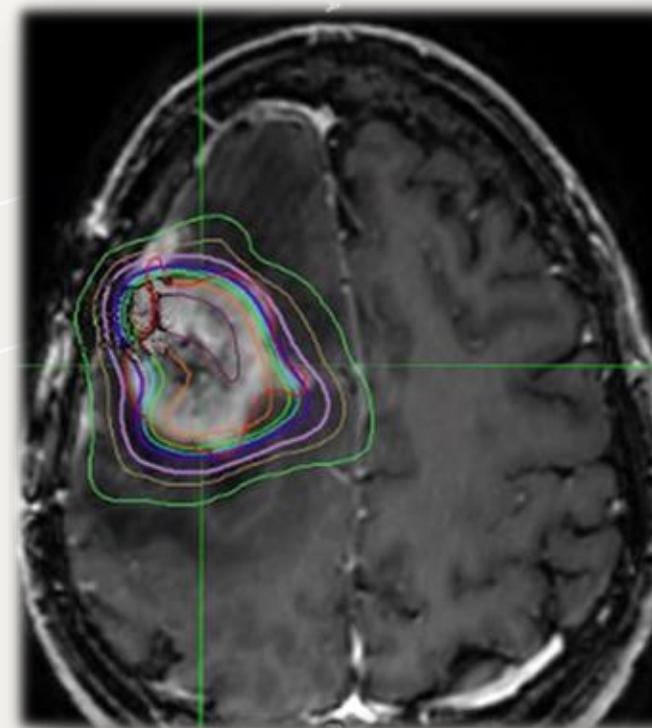
### 30 Doses of EBRT

- + Maximum Dose ~ 30 Gy
- + Poor precision



### 1 Dose of REYOBIQ

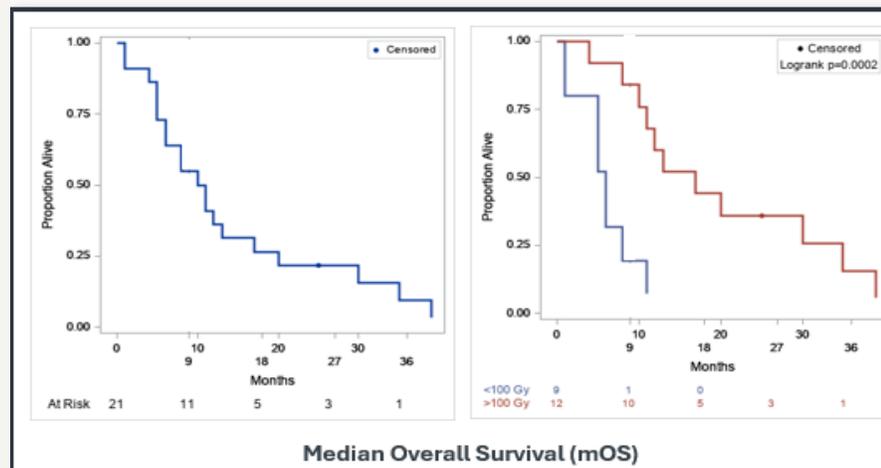
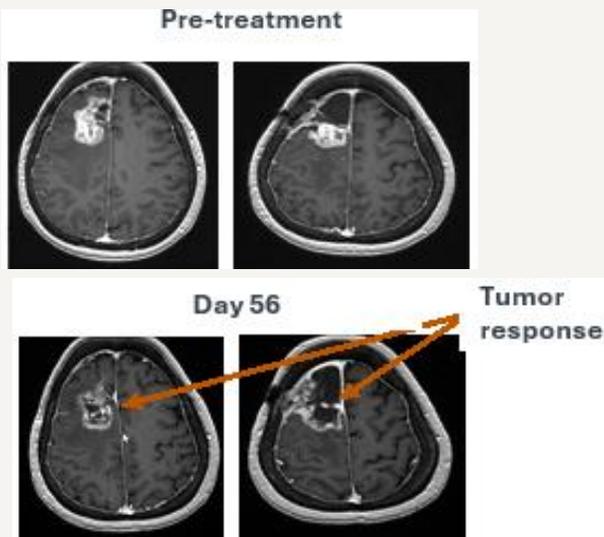
- + Maximum Dose ~ 740 Gy
- + High precision
- + High doses to Infiltrative Margin



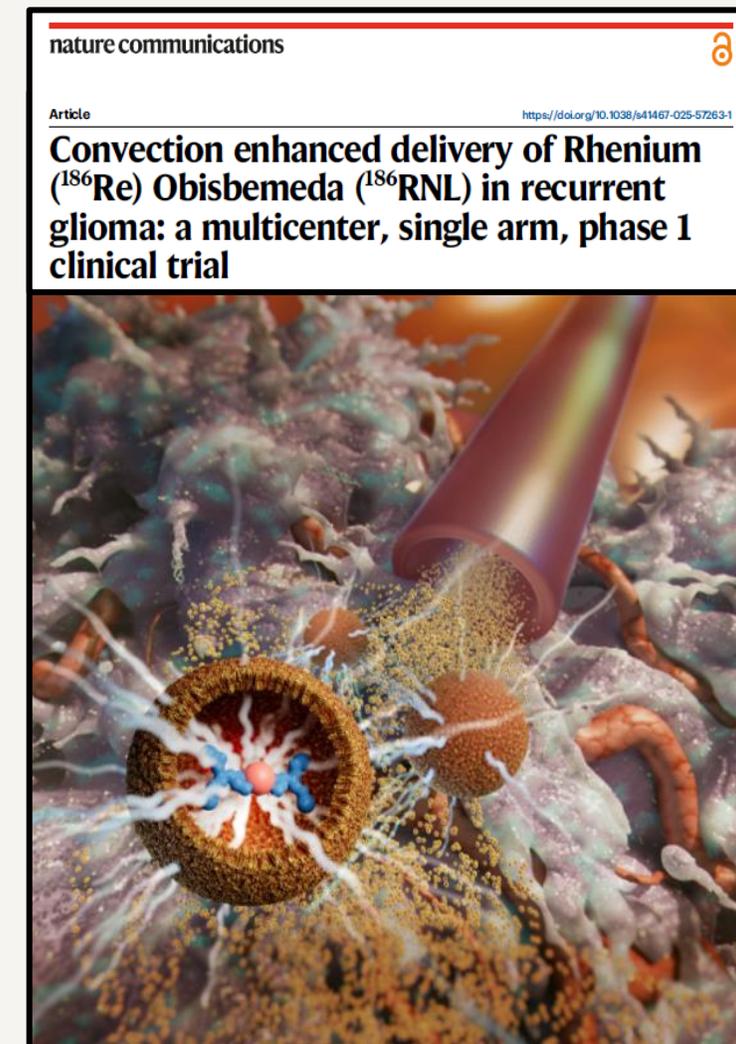
# ReSPECT-GBM Phase 1 Single Administration Dose Escalation Trial

## Positive Data published in NATURE Communications

- + Radiation doses to tumor of up to 740 Gy, average doses greater 300 Gy
- + Clear imaging responses and tumor reduction
- + Patients receiving >100 Gy had 17 months mOS vs 6 months <100 Gy (p=0.001), note-standard of care is 8 months overall survival
- + P1 data analyzed against 2 'real-world' control arms:
  - 38% improvement for the entire population
  - 113% for patients receiving therapeutic dose radiation (> 100 Gy)



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

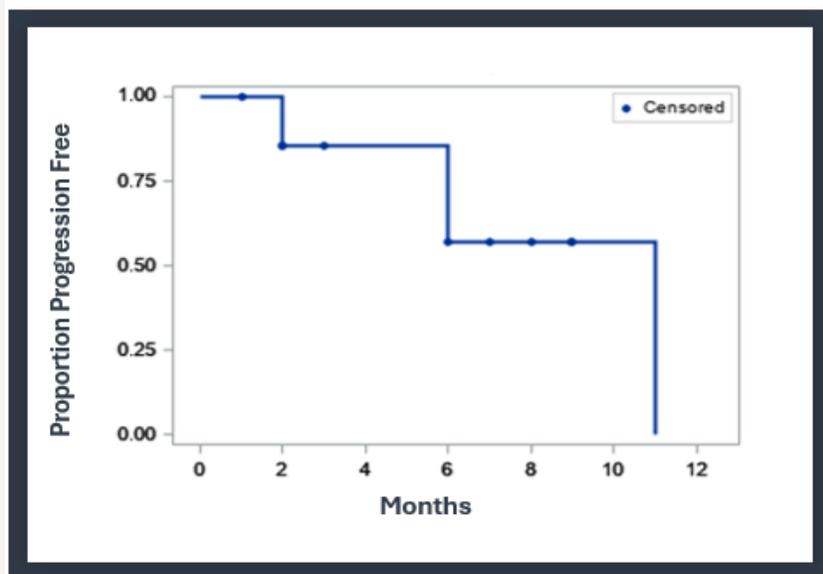


# ReSPECT-GBM Phase 2 Single Administration Dose Escalation Trial

*Interim data in P2 trial shows favorable effect on disease progression & survival*

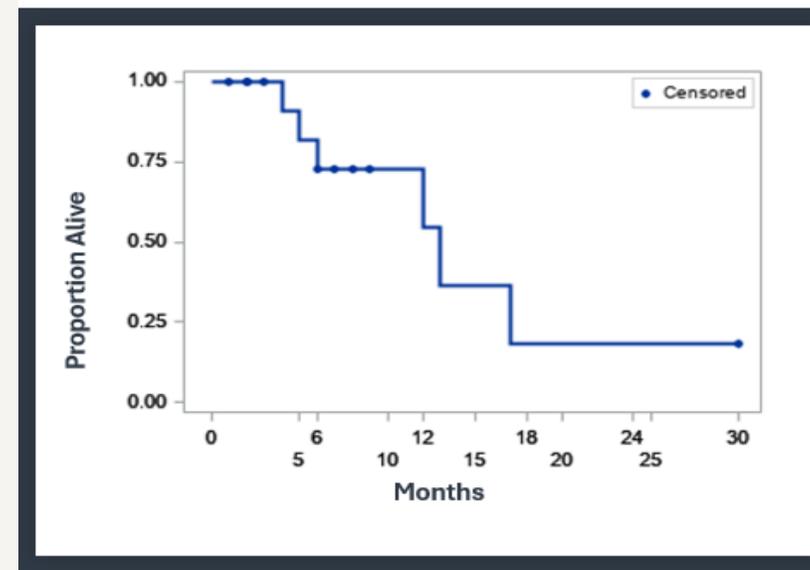
- + 23 (out of 34) patients treated w/RP2D safety profile consistent with Phase 1 data
- + Survival at interim analysis tracking with P1 data
- + P2 data analyzed against 2 ‘real-world’ control arms:
  - 63% improvement in Phase 2 patients (n=15 of 34 planned patients)<sup>1</sup>

**Median Progression Free Survival**



**PFS: 11 months**

**Median Overall Survival**



**OS: 13 months**

# ReSPECT-PBC Phase 1/2 Single Dose Escalation Trial

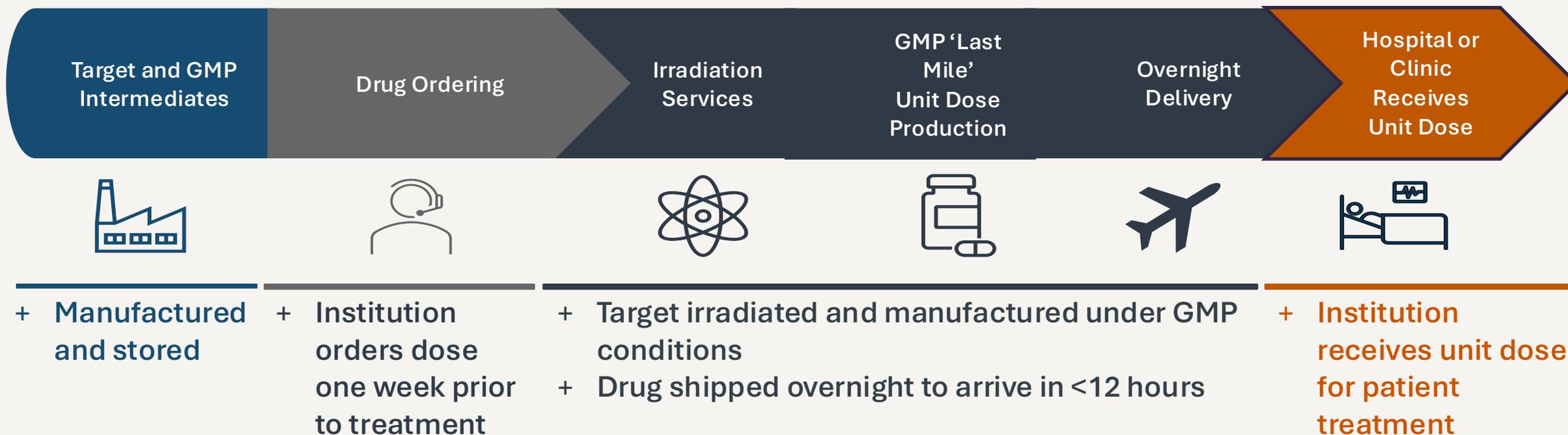
*For the treatment of rare, aggressive pediatric brain cancers*

- + Recurrent, refractory, or progressive ependymoma and high-grade glioma
- + Obtained FDA IND clearance Q2 2025
- + Expect to begin enrollment in 1Q 2026
- + Initial site: Lurie Children's Hospital in Chicago, IL
- + Funded by \$3.0 million award from U.S. Department of Defense



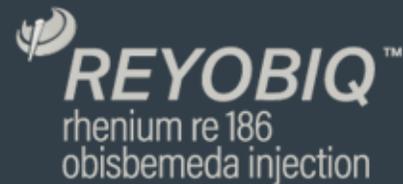
# REYOBIQ Manufacturing Logistics

Scalability in 2026 to meet breadth of clinical and commercial scenarios



# Thank You

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Contact us at [investor@plustherapeutics.com](mailto:investor@plustherapeutics.com)