



Corporate Presentation

March 2024

Forward Looking Statement

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” 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 rhenium (¹⁸⁶Re) obisbameda including the ability of rhenium (¹⁸⁶Re) obisbameda 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; 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 rhenium (¹⁸⁶Re) obisbameda; the continued evaluation of rhenium (¹⁸⁶Re) obisbameda including through evaluations in additional patient cohorts; and the intended functions of the Company’s platform and expected benefits from such functions.

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Targeted Radiotherapeutics for CNS Cancers

Corporate overview



Platform Technology

- + Nanoliposome and Rhenium isotope-based theragnostic pipeline
- + Novel, directly targeted CNS radiotherapy platform
- + Highly scalable supply chain



CNS Cancer Focus

- + Aggregate market opportunity of \$10B for current indications in development
- + Leptomeningeal metastases (LM) has ~250k patients per year with no approved treatments
- + Recurrent glioblastoma (rGBM) occurs in nearly all GBM patients with poor treatment options



Compelling Survival Data

- + Interim rGBM Phase 2 data (n=15): 13 months median OS¹ vs. SOC ~8 months²
- + LM Phase 1 dose escalation (n=18): No DLTs and median OS of 10 months¹ vs. expected SOC ~4 months³



Mid 2025 Cash Runway

- + Sufficient cash runway to fund operations through mid-2025
- + 2 active grants totaling \$25M in support with many others pending



Significant Milestones

- + Completing rGBM Phase 2 in the next 12 months and interim data analysis at SNO 2024
- + Completing LM single dose Phase 1 in 2024 and interim data analysis at SNO 2024
- + Presenting FORESEE LM diagnostic trial data in mid 2024

Recent Press and Partnerships Highlight Accelerating Interest in Radiopharmaceuticals

THE WALL STREET JOURNAL

These Drug Companies Are Going Nuclear to Fight Cancer

Big pharma's investments in nuclear medicine highlight how cancer treatment is shifting to targeted approaches

By [David Wainer](#) [Follow](#)

Feb. 20, 2024 at 6:30 am ET

Innovator	3B Pharmaceuticals	bicycle therapeutics	POINT BIOPHARMA	RayzeBio	PERSPECTIVE THERAPEUTICS	Fusion Pharmaceuticals Inc.
Acquirer	NOVARTIS	BAYER	Lilly	Bristol Myers Squibb	LANTHEUS	AstraZeneca
Date	4/24/2023	5/10/2023	10/3/2023	12/26/2023	1/9/2024	3/19/2024
Deal Type	License Deal	Strategic Collaboration	Company Acquisition	Company Acquisition	License Deal	Company Acquisition
Aggregate Value	\$425M	\$1.7B	\$1.4B	\$4.1B	\$61M	\$2.4B
Key Deal Terms	<ul style="list-style-type: none"> \$40M upfront Development, regulatory, and commercial-based milestones (\$425M) Tiered royalties 	<ul style="list-style-type: none"> \$45M upfront Development and commercial-based milestones (\$1.7B) Mid-single to double-digit tiered royalties 	<ul style="list-style-type: none"> \$12.50/share - 87% premium 	<ul style="list-style-type: none"> \$62.50/share - 104% premium 	<ul style="list-style-type: none"> \$28M upfront \$33M equity investment (19.9% of outstanding shares) 	<ul style="list-style-type: none"> \$21.00/share - 97% premium \$2B upfront CVR \$3.00/share contingent on specified reg. milestone

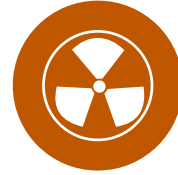
Unique Challenges with CNS Cancer Treatment

Plus' technology overcomes all key challenges



Blood Brain Barrier

Only 2% of drugs cross the BBB



Radiotherapy Limitations

EBRT dose limited by off target safety concerns



Locally Invasive

90% of GBM recurs 2 cm from primary tumor



Chemoresistance

MGMT status and acquired resistance



Surgical Therapy Inadequate

Clean surgical margins unobtainable



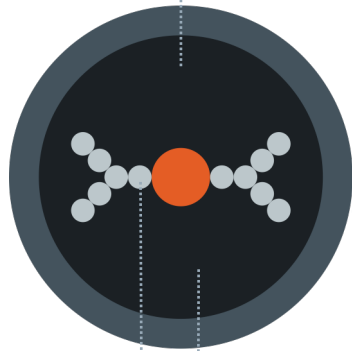
Complex Anatomy

Getting 'drug on tumor' more difficult

Rhenium (^{186}Re) Obisbameda is a 3-Part Formulation Radiotherapy

Improves CED and prolongs radiation exposure to tumor while sparing healthy tissue

Rhenium-186
(^{186}Re)



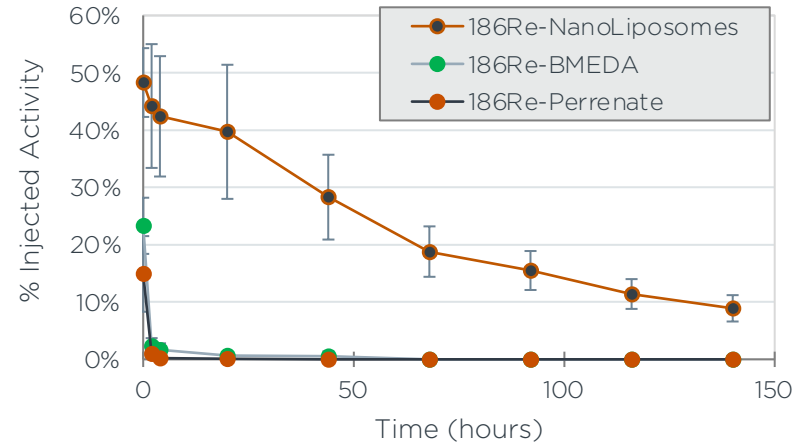
BMEDA Small Molecule

Chelates ^{186}Re before loading into the nanoliposome where it is irreversibly trapped

100 nm Nanoliposome

Carries BMEDA- ^{186}Re to target tumor and improves retention

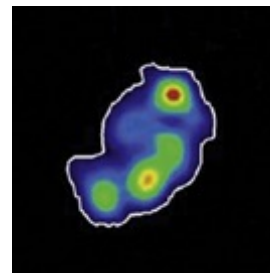
Tumor Retention



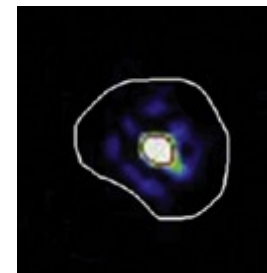
Proprietary formulation promotes persistence in the tumor throughout the decay cycle of the isotope

Improved Drug Distribution

$^{99\text{m}}\text{Tc}$ +NanoLiposome



$^{99\text{m}}\text{Tc}$ -BMEDA only



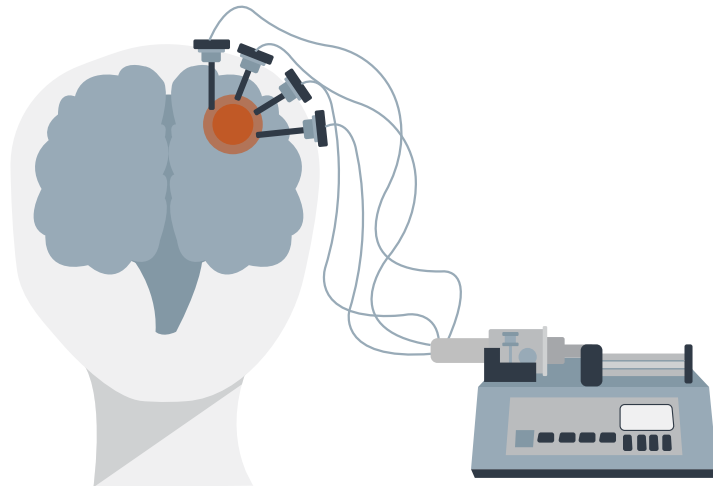
Proprietary formulation improves convection and distribution throughout the brain

Direct Radiotherapeutic Delivery Strategies for CNS Cancers

Overcomes barriers to CNS drug delivery

Convection-Enhanced Delivery (CED)

- + FDA-approved and utilized for 20+ years
- + Bypasses BBB
- + 'Biological fracking': Controlled pressure and flow are optimal for drug delivery to region of interest
- + Utilized for GBM and other brain tumors



Brain Parenchyma

Intraventricular Catheter (Ommaya reservoir)

- + FDA-approved and utilized for 60+ years
- + Bypasses BBB
- + Small subcutaneous reservoir with direct ventricle access
- + Allows multidosing and CSF sampling
- + Commonly placed in LM patients



Cerebrospinal Fluid

A New Paradigm for CNS Radiotherapy

A direct targeted approach is a step function improvement in CNS radiation delivery

Gold Standard

External Beam Radiation Therapy



- + Standard of care for decades
- + Requires fractionation
- + Limited absorbed dose due to off-target toxicity
- + Mature technology

New Paradigm

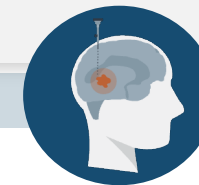
Plus' Directly Targeted RT Delivery



- + Direct delivery to the tumor site
- + Key challenges eliminated
- + Monitor drug location with real-time imaging
- + Quantify absorbed doses
- + Safe delivery of high activity



Imaging & Pre-Treatment Planning



Biopsy & Catheter Placement



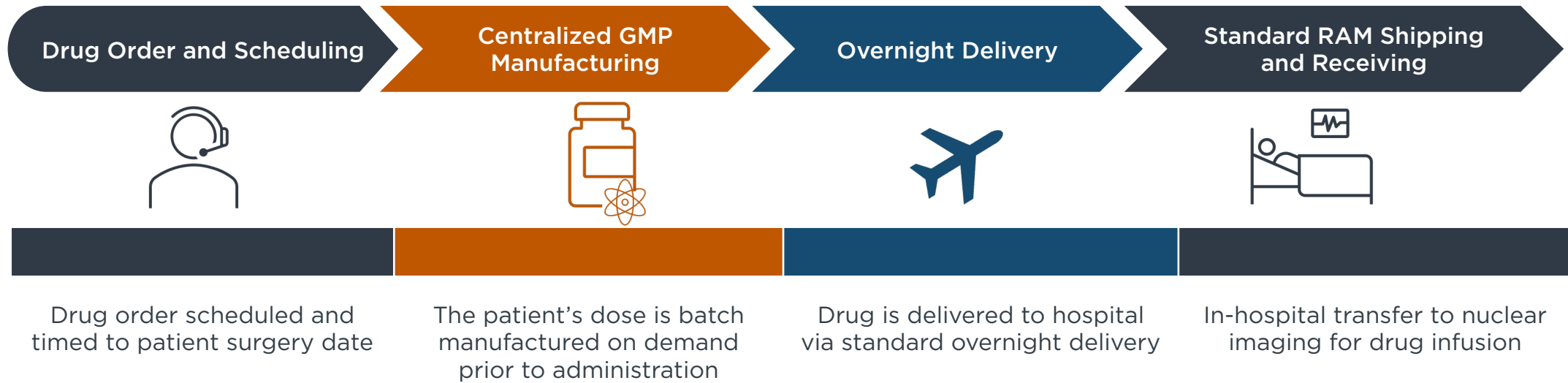
Convection Enhanced Delivery



Dosimetry & Imaging

Seamless drug supply into patient workflow

Highly scalable workflow to meet commercial demand



Therapeutic Product Pipeline

Status and 2024 milestones

		Preclinical	IND/ IDE	Phase 1	Phase 2	Phase 3	Anticipated Milestones 2024
Rhenium (¹⁸⁶Re) Obisbameda							
Leptomeningeal Metastases	Single dose administration trial	ReSPECT-LM Single Dose Trial					<ul style="list-style-type: none"> Data presentation at SNO Nov 2024 Begin P2 in breast cancer
	Multidose trial	ReSPECT-LM Multidose Trial					<ul style="list-style-type: none"> Initiate P1 basket trial
Malignant Gliomas	Recurrent glioblastoma for small-to-medium sized tumors	ReSPECT-GBM					<ul style="list-style-type: none"> Complete enrollment (n=34) Interim data at SNO Nov 2024 Confirm pivotal trial design
	Pediatric high-grade glioma and ependymoma	ReSPECT-PBC					<ul style="list-style-type: none"> IND approval & initiate enrollment
Rhenium NanoLiposome Biodegradable Alginate Microsphere (RNL-BAM)							
Various Solid Tumors	Primary and Secondary Liver Cancer						<ul style="list-style-type: none"> Formulation optimization
CNS tumors	Glioblastoma						<ul style="list-style-type: none"> Proof-of-concept studies

Leptomeningeal Metastases

Power and precision in
cancer radiotherapeutics



Leptomeningeal Metastases from Solid Tumors

Poor prognosis and no FDA-approved treatments

LM Diagnosis

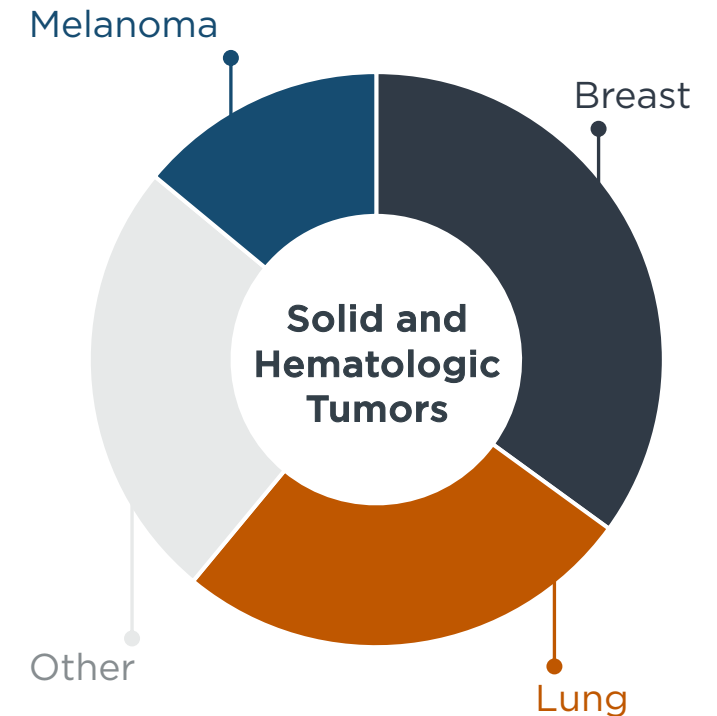
- + **Late-stage cancer complication** in which cancer cells metastasize from primary tumor to the CSF space and leptomeninges
- + **Increasing incidence** with ~155,000 U.S. patients per year (5-8% of those with solid tumors)
- + **Likely 2-4x underdiagnosed** based on autopsy findings¹

LM Treatment

- + **Poor survival** of 4-6 weeks without treatment
- + **No approved therapies**
- + **No standard of care;** treatments (systemic therapy for primary cancer and craniospinal-directed chemo and radiation) may relieve symptoms, but do not halt disease progression nor impact survival

Opportunities:

- + First-in-class radiotherapeutic with a targeted dose delivered in a single outpatient administration
- + First-in-class highly sensitive and specific diagnostic to monitor disease and therapy



Leptomeningeal Metastasis Incidence

Approximately 250,000 new cases of LM are diagnosed each year in the US

Primary Tumor Type	U.S. Incidence (% solid tumors)	Standard of Care: Median Overall Survival	Patients
Breast	12-34%*	3.5-4.4 months	~210,000
Lung	10-26%*	3-6 months	~130,000
Melanoma	17-25%*	1.7 to 2.5 months	~45,000
Other Cancer	5%*	2-4 months	~200,000

- + *Le Rhun, E., et. al. (2013). Surgical neurology international. <https://doi.org/10.4103/2152-7806.111304>
- + ~300,000 new breast cancer cases estimated to be diagnosed in US in 2024 (<https://www.cancer.org/cancer/types/breast-cancer/about/how-common-is-breast-cancer.html>)
- + ~240,000 new lung cancer cases estimated to be diagnosed in US in 2024 (<https://www.cancer.org/cancer/types/lung-cancer/about/key-statistics.html>)
- + ~100,000 new melanoma cases estimated to be diagnosed in US in 2024 (<https://www.cancer.org/cancer/types/melanoma-skin-cancer/about/key-statistics.html>)
- + ~1.3M other cancers diagnosed in US in 2023 (<https://seer.cancer.gov/statfacts/html/common.html>)
- + 2-4X underdiagnosed

ReSPECT-LM Phase 1 Single Dose Escalation Trial

Targeted delivery of Rhenium (¹⁸⁶Re) Obisbameda to CSF by Ommaya reservoir

- + **Dose escalation:** 3+3 modified Fibonacci
- + **Primary objective:** Safety and tolerability
 - + Maximum Tolerated Dose / Maximum Feasible Dose
- + **Secondary objectives:** Efficacy
 - + Overall Response Rate (ORR)
 - + Duration of Response (DoR)
 - + Progression Free Survival (PFS)
 - + Overall survival (OS)
- + **Exploratory objectives:** Analysis on cerebral spinal fluid (CSF) pre- and post-administration
 - + CSF tumor cell enumeration
 - + Pharmacodynamic (PD) markers
 - + QoL assessments
- + **Funding:** \$17.6M grant from largest state funding agency (CPRIT)

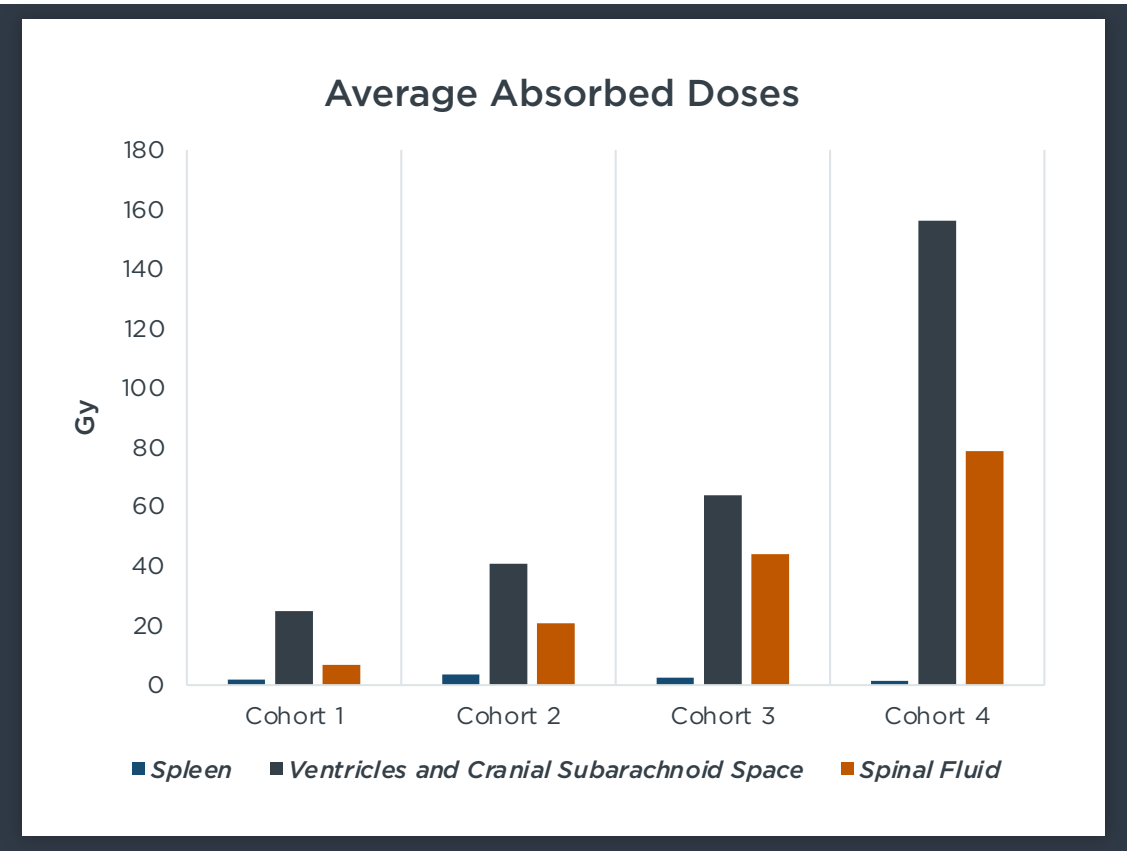
Single Administration Phase 1 Dose Escalation Plan

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
CURRENT 6	5	87.97	17.59
7	5	109.96	21.99

ReSPECT-LM Safety

MTD/MFD not reached over 5 cohorts

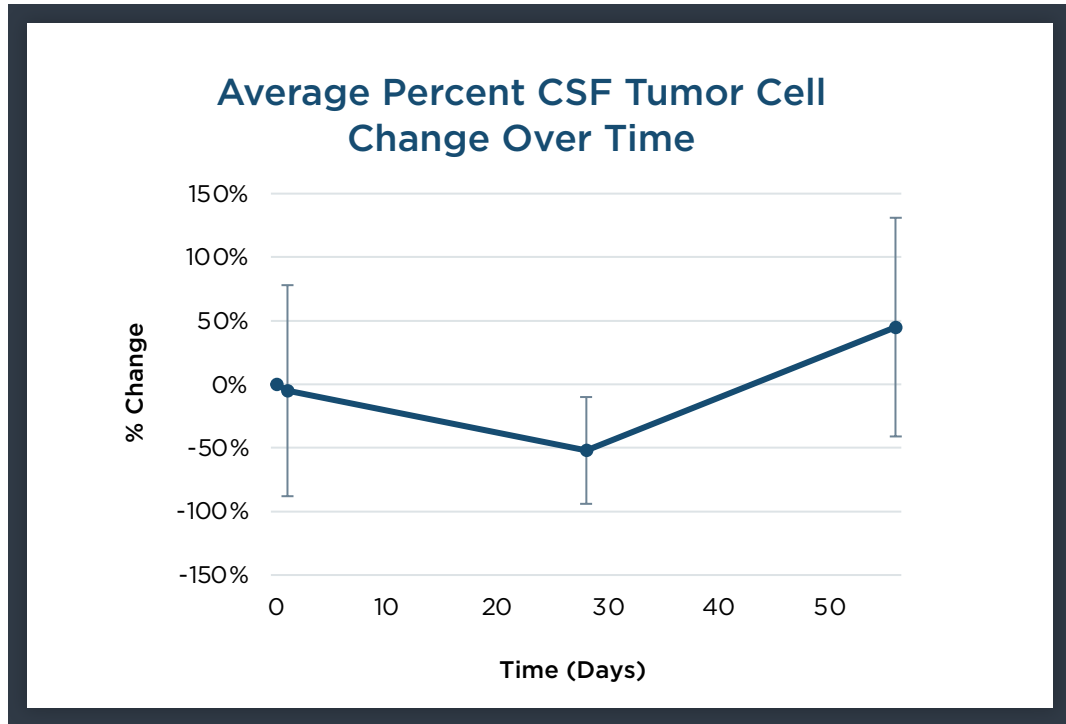
- + Generally safe and well tolerated
- + Complete CSF circulation of drug within hours and duration at least 7 days
- + No evidence of systemic radiation toxicity
- + Absorbed doses to key therapeutic areas increase with administered dose
- + Absorbed doses to critical organs remains low
- + All but one SAE unrelated to study drug



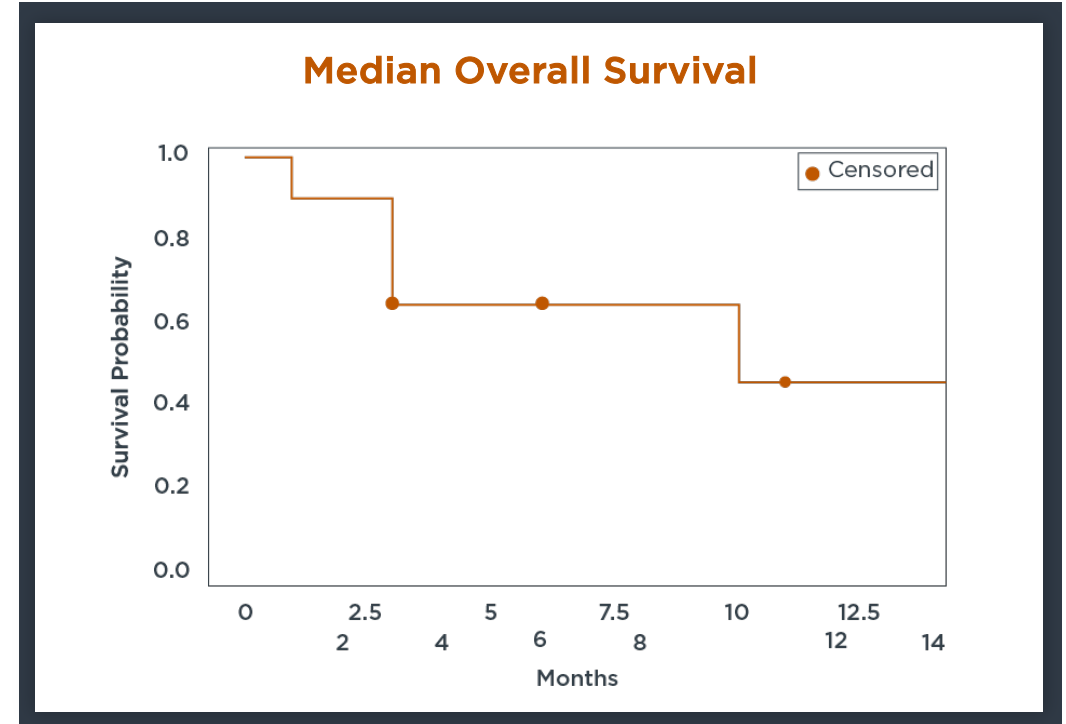
Trial Safety Summary				
Grade	%	n	>5% AEs	SAEs
Grade 1	64.10%	(68)		
Grade 2	27.35%	(31)		
Grade 3	7.27%	(8)	Headache (5.45%)	5
Grade 4	0.91%	(1)		
Grade 5	0.91%	(1)		

ReSPECT-LM Phase 1 Treatment Response Data

Median overall survival and percent CSF tumor cell change show potential treatment effect



- + N = 13 evaluable patients
- + Max percent reduction in CSF tumor cells at D28 was 90%
- + Average of 53% CSF tumor cell reduction at D28



- + N = 10 patients, cohorts 1-3
- + mOS was 10 months*
- + 5 of these patients remain alive**

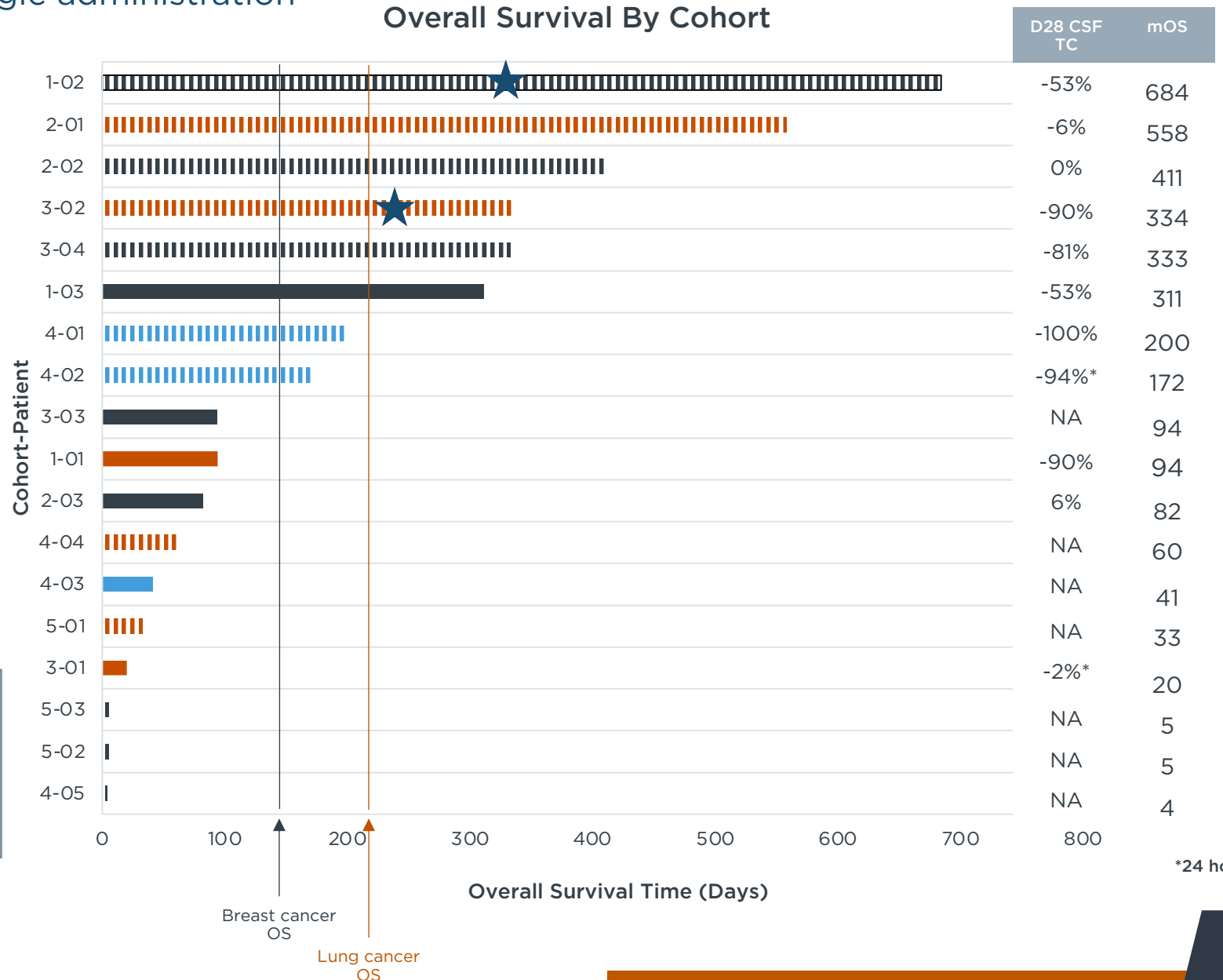
ReSPECT-LM Individual Patient Analysis

Analysis by survival time following single administration

- + N = 18 evaluable patients
- + 12 of 18 patients alive
- + Tumors by primary disease
 - + Lung: 6
 - + Breast: 9
 - + Other: 3
- + 2 patients received compassionate use 2nd dose

LEGEND

- **Black:** breast primary cancer
- **Orange:** lung primary cancer
- **Blue:** other primary cancer
- **Hatched fill:** Alive
- **Solid fill:** Deceased
- **Star:** Retreatment date



CNSide Tumor Cell Enumeration Assay

Highly sensitive and specific test of metastatic carcinomas in the CSF

Proprietary Technologies

CSF collection & transport system

- Stable at ambient temperature (4 days)
- Preserves membrane antigens



CEE-Sure collection system

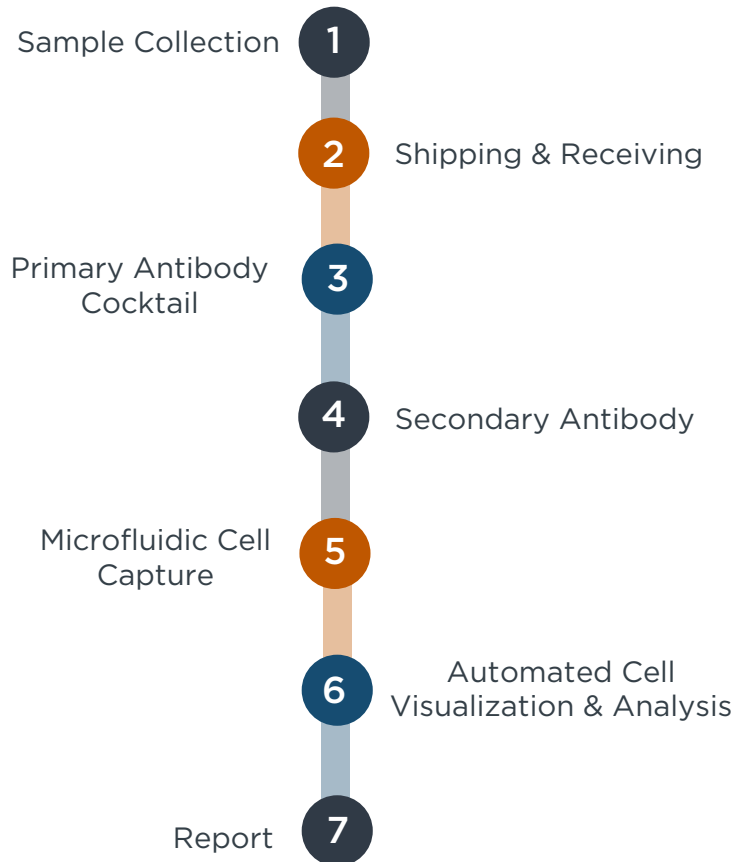
Cell enumeration testing

The CNSide test is designed to quantitate CSF tumor cells originating from breast, GI, cervix, kidney, lung, pancreas, prostate and stomach or melanomas originating from skin.

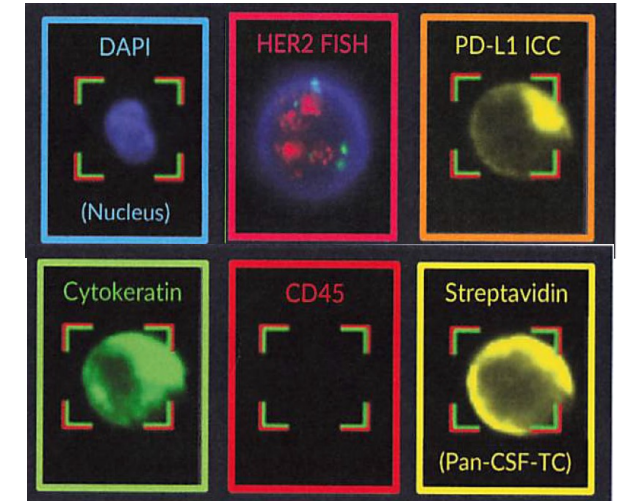
Monoclonal Antibody Cocktail

EpCAM, MET, SUSD2, Trop2, MUC1, CD318, HER2, FOLR1, MCAD, EGFR

Proprietary Testing Process



Individual Cell Data



CNSide assay available for

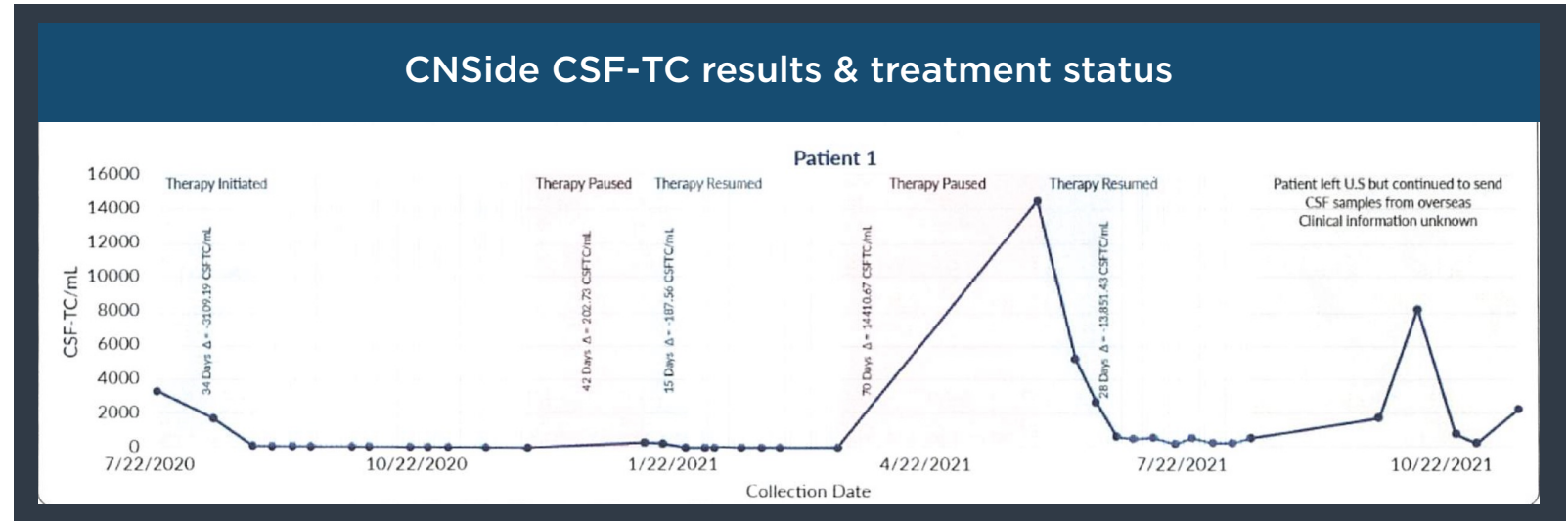
ReSPECT-LM trial

as of Q1 2024

CNSide Clinical Impact and Next Steps

FORESEE clinical feasibility trial enrolled and data readout pending

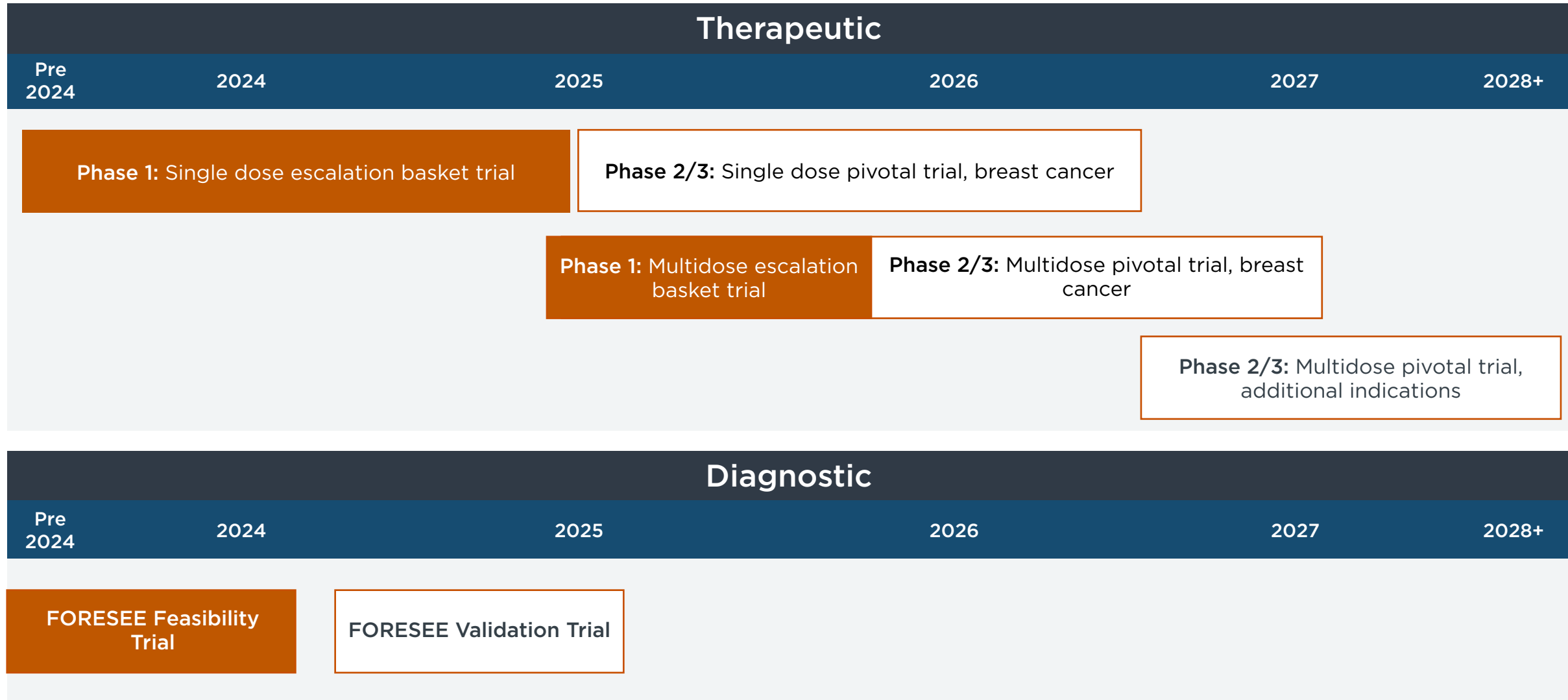
- + CNSide test available commercially and reimbursed prior to Q3 2023
- + FORESEE Clinical Trial (NCT0541123) now enrolled
 - + Prospective multicenter trial
 - + N = 40 patients
 - + Primary endpoint: Determine the impact of CNSide in combination with MRI, cytology, and clinical evaluation on clinical decision making
 - + Secondary: Correlate TCs with LM clinical response and cytology
 - + Data anticipated mid 2024
- + Next steps:
 - + Publication FORESEE data
 - + Reinstate CLIA certification
 - + Seek inclusion in NCCN guidelines
 - + Re-launch commercial testing in 2025



Clinical Impact- single patient longitudinal follow up

ReSPECT-LM and CNSide Pipeline

Clinical development timelines



Recurrent Glioblastoma

Power and precision in
cancer radiotherapeutics



Malignant Gliomas

The brain's most frequent and deadly tumors despite decades of research

GBM Diagnosis

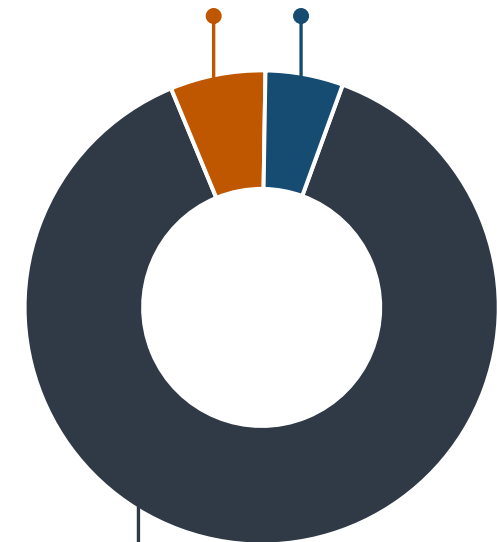
- + 14,500 patients newly diagnosed GBM patients in US each year
- + Poor survival rate, 7% at 5 years
- + Almost all reoccur several months from surgery
- + Poor survival after recurrence, ~8 months mOS

GBM Treatment

- + No standard of care following recurrence
- + Only 5 FDA-approved therapies in the last 50 years
- + Clinical trial recommended by NCCN guidelines for CNS cancers upon recurrence

Opportunities: Treat **adult & pediatric malignant gliomas** with a first-in-class targeted radiotherapeutic that directly delivers high-dose radiation to the tumor while sparing healthy tissue

Ependymoma Oligodendroglioma



Astrocytoma
GBM
Pediatric High-Grade Glioma
Pediatric DIPG

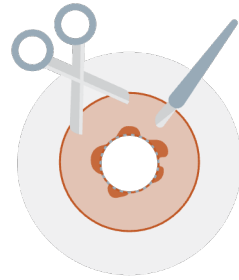
Rhenium (^{186}Re) Obisbameda for Glioblastoma

PLUS' novel approach overcomes limitations of all 3 currently employed treatment modalities

GBM Tumor Pathophysiology
Extremely Difficult to Treat

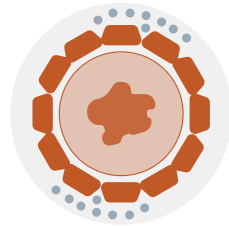


Infiltrative Margin
90% recurrences: 2 cm



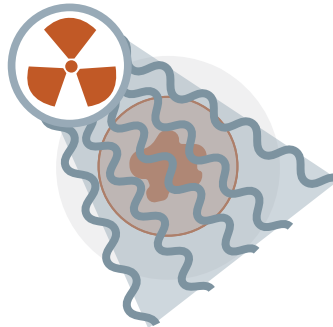
Surgery

Obtaining adequate surgical margins nearly impossible



Systemic Drugs

Only 2% of drugs pass the BBB

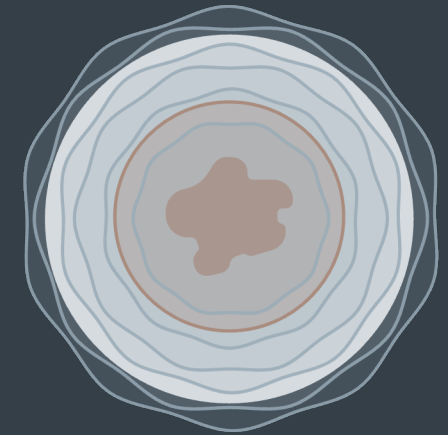


External Beam Radiation Therapy

Inadequate tumoricidal doses because of toxicity to healthy brain tissue

PLUS

Rhenium (^{186}Re) Obisbameda

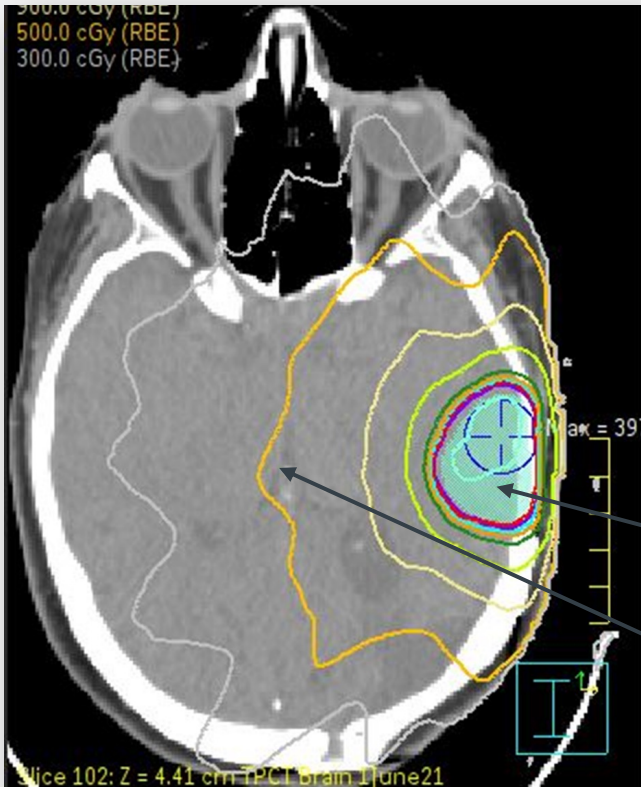


Goal- treat both tumor and infiltrative margin with at least 100 Gy radiation

Rhenium (^{186}Re) Obisbameda Advantage Over EBRT

More targeted radiation delivery with 10x increase in max absorbed dose

EBRT

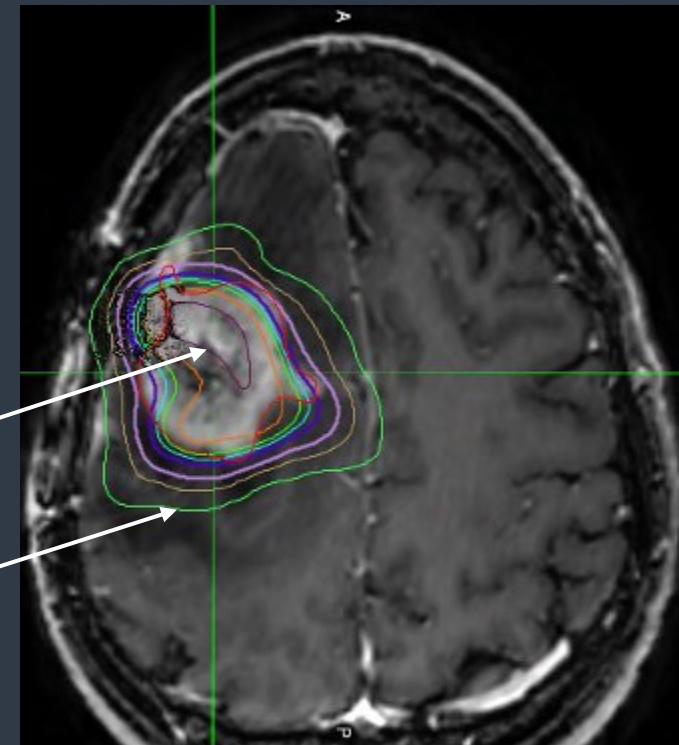


28.5 Gy
Max dose
5 Gy

EBRT vs. Rhenium (^{186}Re) Obisbameda

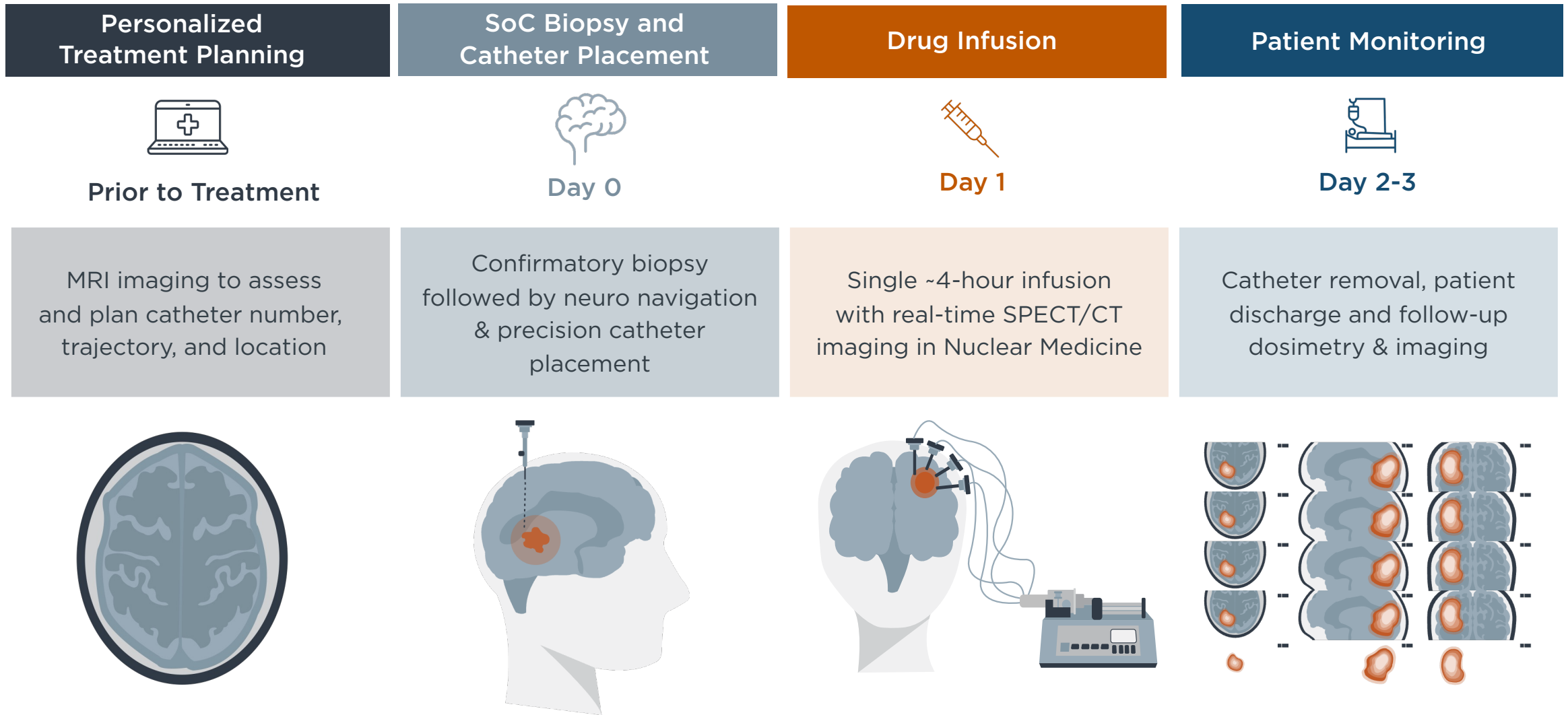
250 Gy
Max dose
5 Gy

Rhenium (^{186}Re) Obisbameda



ReSPECT-GBM Treatment Workflow

Inpatient single administration



ReSPECT-GBM Phase 1, Single Dose Trial Design

Single administration of Rhenium (^{186}Re) Obisbameda 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

Single Administration Phase 1 Dose Escalation Plan

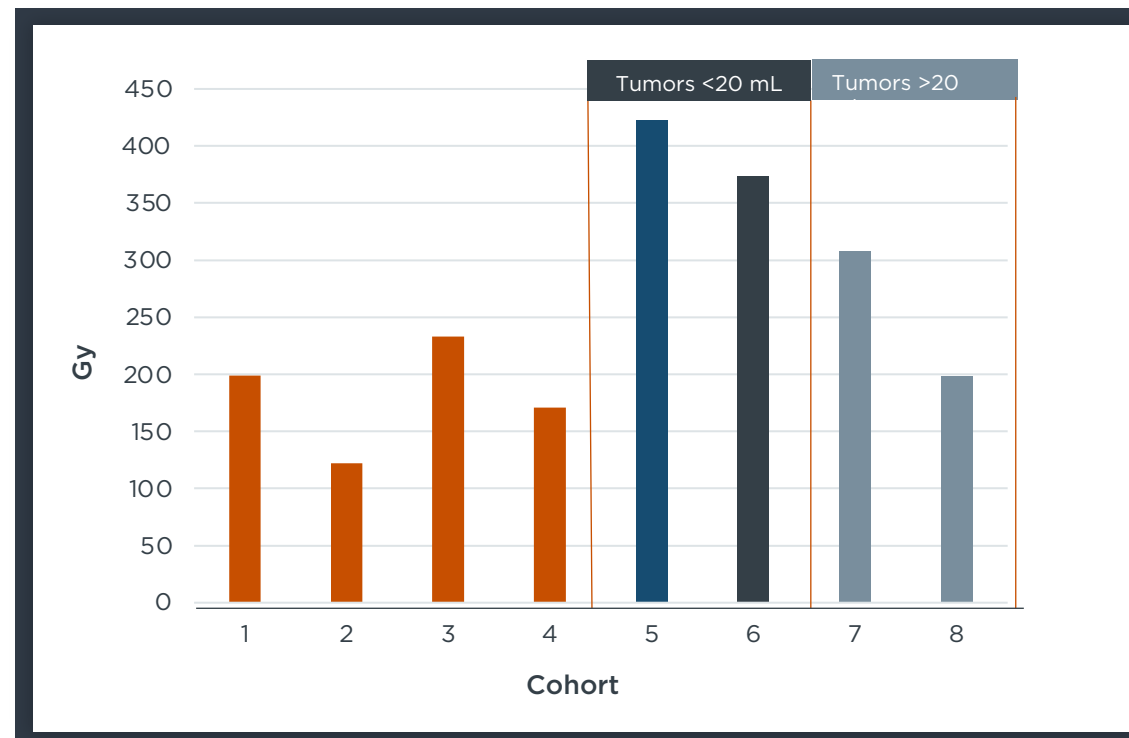
Cohort	Administered Volume (mL)	Administered Activity (mCi)	Administered Concentration (mCi/mL)
1	0.66	1.0	1.5
2	1.32	2.0	1.5
3	2.64	4.0	1.5
4	5.28	8.0	1.5
5	5.28	13.4	2.5
RP2D	6	8.80	2.5
	7	12.3	2.5
Current	8	16.34	2.5

ReSPECT-GBM Safety

MTD/MFD not reached in dose escalation phase

- + Generally safe and well tolerated over 28 patients in 8 dosing cohorts, enrollment ongoing
- + No evidence of systemic radiation toxicity
- + The average absorbed dose to the tumor for all Phase 1 patients was 264 Gy (range: 8.9-739.5 Gy)
- + Most Phase 1 adverse events (AEs) were mild or moderate and resolved with treatment
- + Average absorbed dose to the tumor (n=15) of 309 Gy
- + Increasing tumor size lowers absorbed dose (cohorts 7 & 8)
- + Phase 2 safety profile tracks with Phase 1

Average Absorbed Dose to Tumor by Cohort

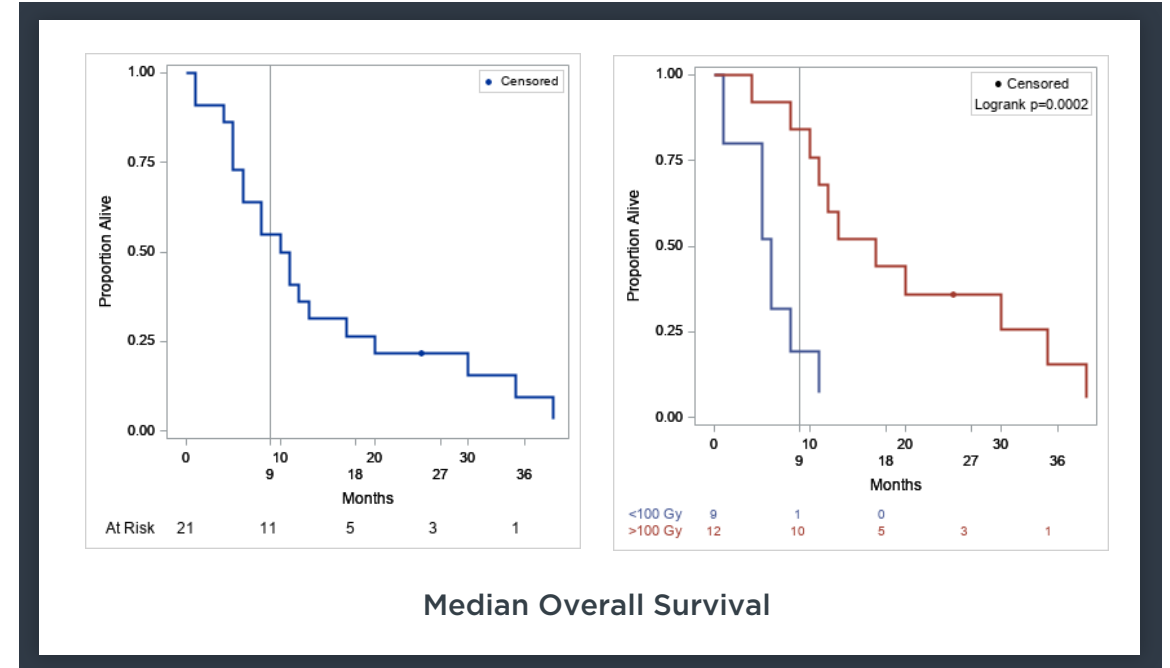
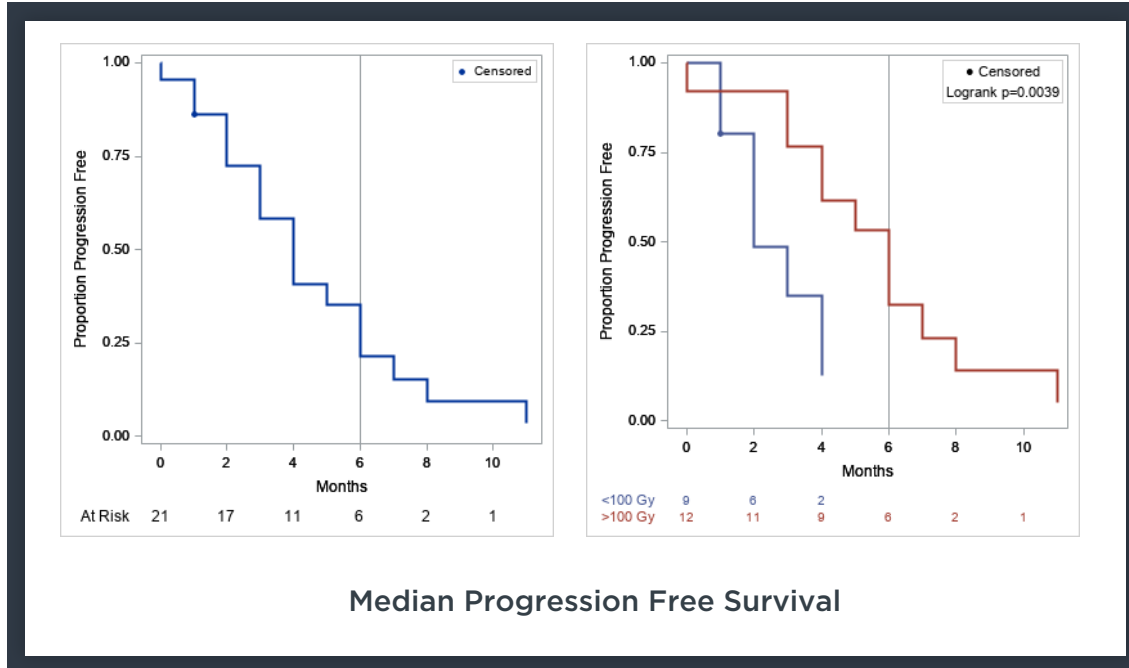


Trial Safety Summary

Grade	>5% AEs	SAEs
Grade 1 66.67% Grade 2 25.71% Grade 3 7.62%	Headache (6.67%) Fatigue (5.24%)	17

ReSPECT-GBM Phase 1 Efficacy

Dichotomous patient stratification of patients based on 100Gy absorbed dose threshold



Progression free survival or PFS

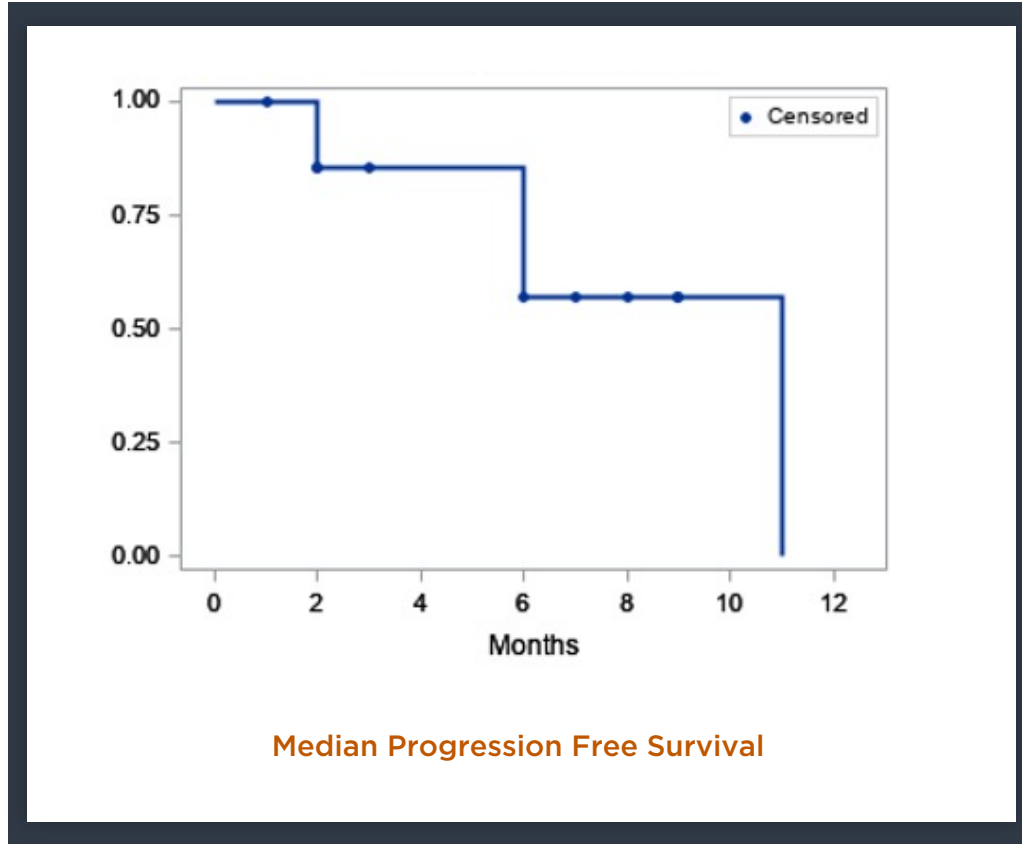
- + All patients: mPFS 4.0 m (95% CI 2.0-6.0 m, PFS6=0.21±0.11)
- + Patients with <100 Gy: mPFS of 2.0 m (95% CI 1.0-4.0 m, PFS6=0.0) (blue)
- + Patients with ≥100 Gy: mPFS of 6.0 m (95% CI 3.0-8.0 m, PFS6=0.32±0.16) (red)

Median overall survival or mOS

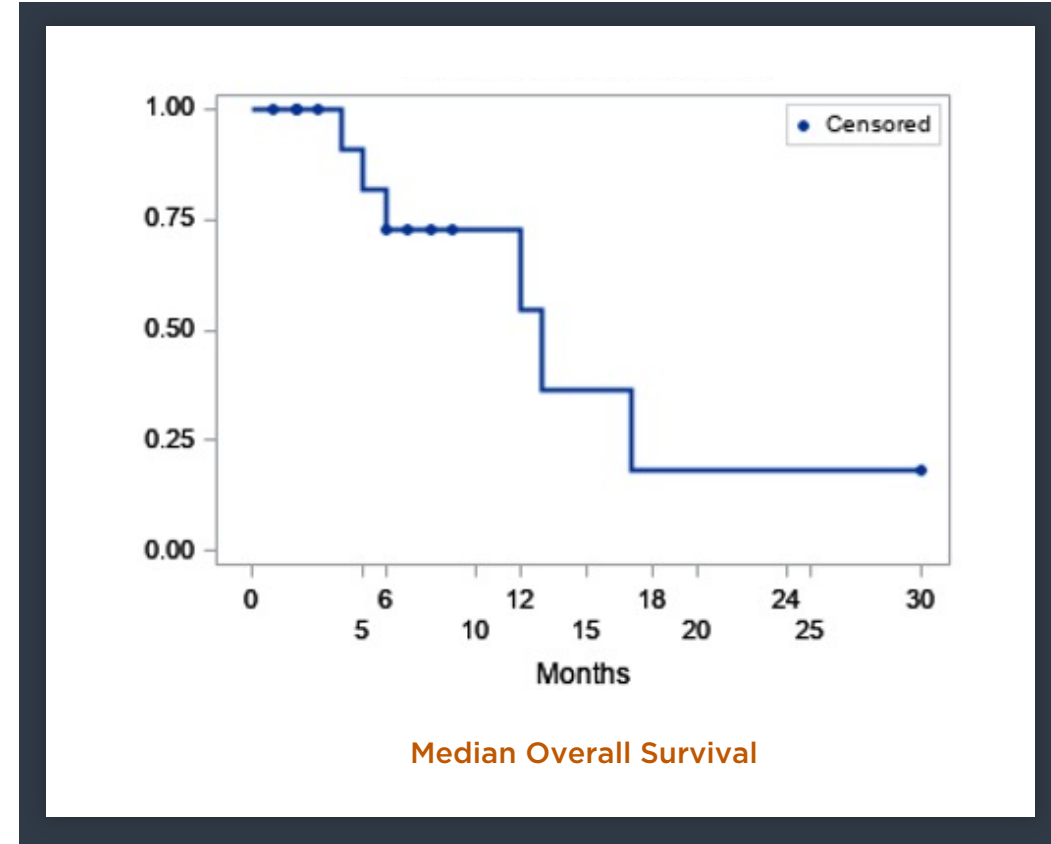
- + All patients: mOS was 11.0 m (95% CI 5.0-17.0 m, OS9=0.55±0.11)
- + Patients with <100 Gy: mOS of 6.0 m (95% CI 1.0-11.0 m, OS9=0.19±0.18) (blue)
- + Patients with ≥100 Gy: mOS of 17.0 m (95% CI 8.0-35.0 m, OS9=0.84±0.11) (red)

ReSPECT-GBM Phase 2 Efficacy

Phase 2 data similar to Phase 1 data receiving therapeutic radiation dose



+ **mPFS:** 11 months (95% CI 6-11 months)

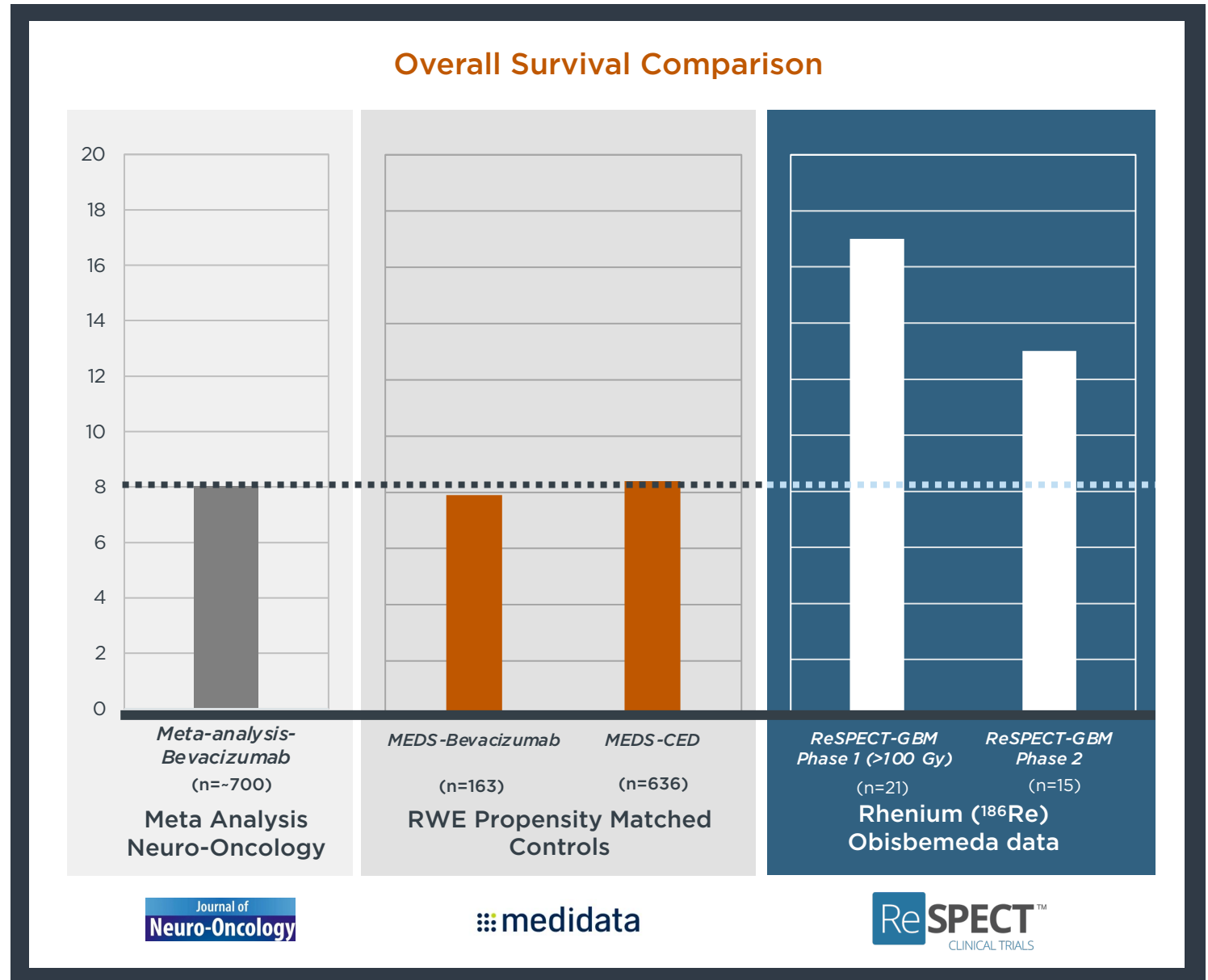


+ **mOS:** 13 months (95% CI 5 months-NA)

Comparative Survival Data

ReSPECT-GBM vs. Real World Experience

- + Meta analysis of ~700 rGBM patients
- + Plus and Medidata conducted 2 RWE control arms with propensity match rGBM patients to Plus Phase 1 data
- + Propensity matching- baseline characteristics were well-aligned
- + 38% improvement over RWE control for Phase 1 (to RP2D)
- + Respect GBM phase 1 N = 21, phase 2 N = 15 (6 alive**)
- + 113% improvement over RWE control in patients receiving therapeutic dose radiation (>100Gy)
- + 63% improvement in Phase 2 patients (n=15 of 34 planned patients)



ReSPECT-PBC

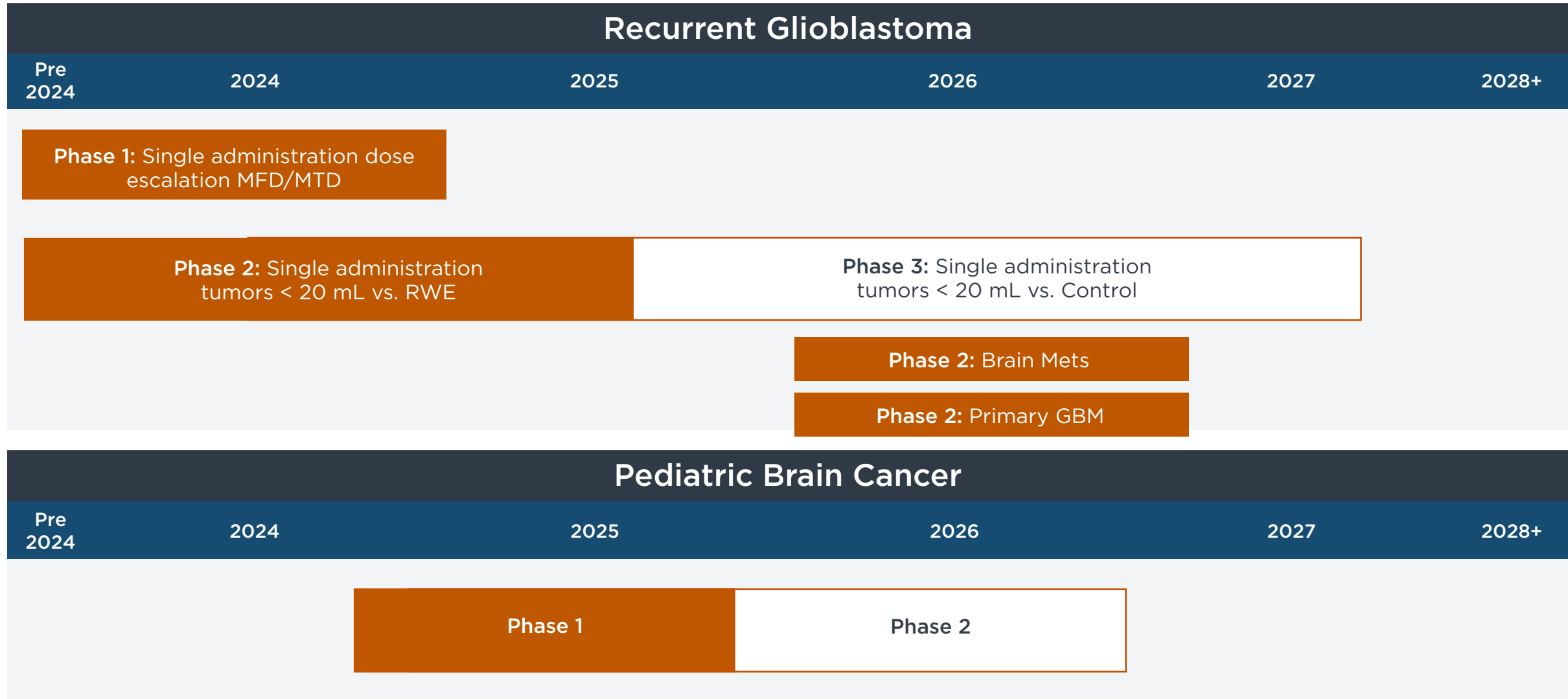
Rhenium (¹⁸⁶Re) Obisbameda for supratentorial recurrent, refractory, or progressive pediatric high-grade glioma and ependymoma

- + **Dose escalation:** 3+3 modified Fibonacci, varying administered volume with tumor volume to maximize therapeutic effect
- + **Primary objective:** Safety and tolerability
 - + Maximum Tolerated Dose / Maximum Feasible Dose
- + **Secondary objectives:** Efficacy
 - + Dose distribution
 - + Neuropsychologic outcomes
 - + Overall Response Rate (ORR)
 - + Progression Free Survival (PFS)
 - + Overall survival (OS)

Cohort	Tumor Volume (mL)	Administered Volume (mL)	Administered Activity (mCi)	Administered Concentration (mCi/ml)
A	0.5	1.4	0.7	0.5
	1.8	2.7	1.35	0.5
	4.2	4.7	2.35	0.5
B	8.2	7.5	7.5	1
	14.1	11.2	11.2	1
	22.4	15.9	15.9	1

ReSPECT-GBM and ReSPECT-PBC Pipeline

Clinical development timelines





Selective Internal Radiotherapy (SIRT) for Solid Tumors

Power and precision in
cancer radiotherapeutics



SIRT (Selective Internal Radiotherapy)

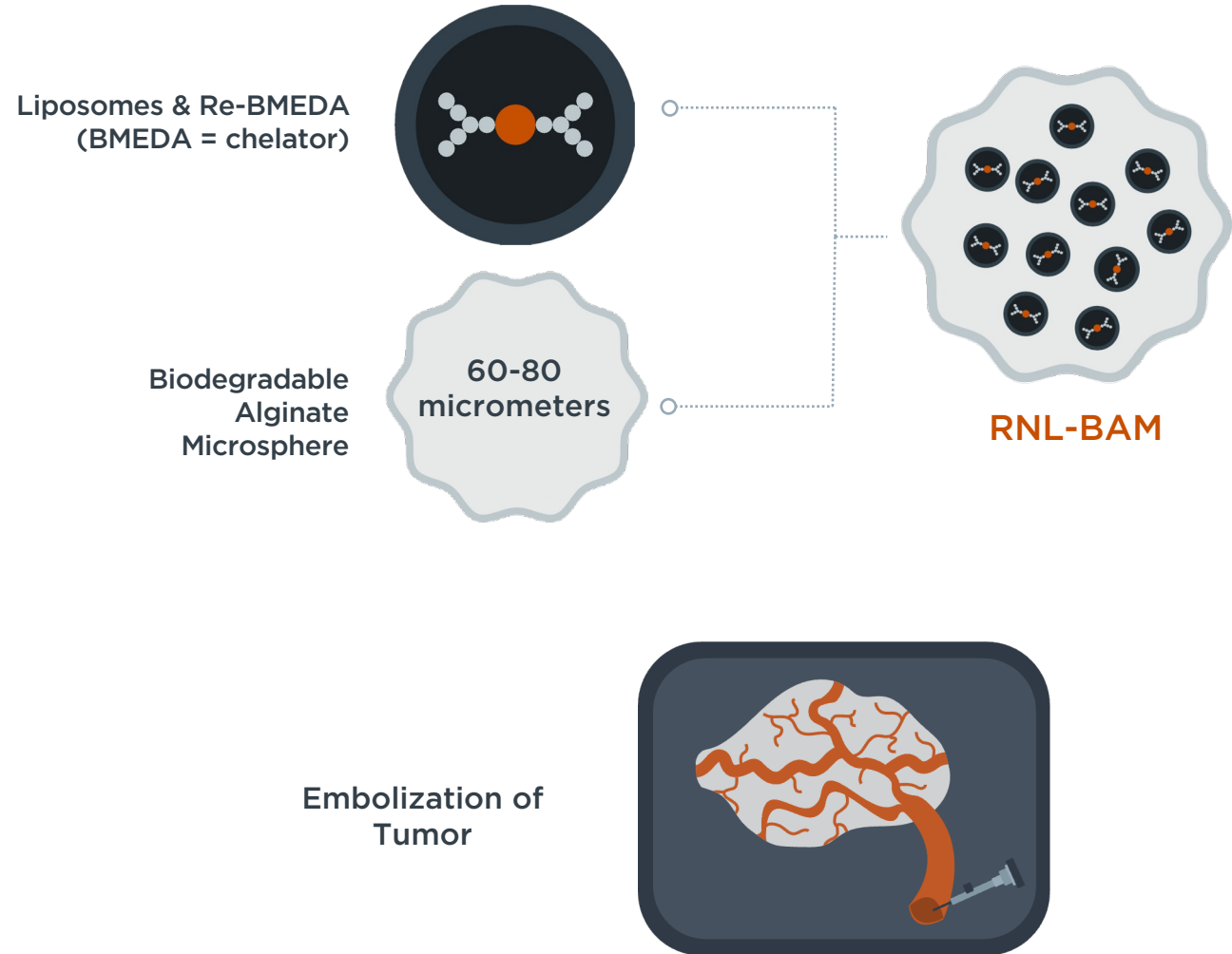
Rhenium NanoLiposome Biodegradable Alginate Microsphere (RNL-BAM) is a next-generation SIRT technology

Current Market

- + Inoperable liver tumors: primary & metastatic disease
- + Regulated as devices
- + TheraSpheres and SIR-Spheres
- + Permanent implants
- + Poor visibility of drug location
- + > \$1B market opportunity for liver only

PLUS Product Differentiation

- + Bioresorbable- allows retreatment
- + Regulated as a device
- + Theragnostic (beta and gamma energy)
- + Visible on angiography
- + Substantial upside potential for liver & other organs, including brain



Financials and Milestones

Power and precision in
cancer radiotherapeutics



Capitalization Summary

As of December 31, 2023

Balance Sheet	Expected Runway	Grant Funding	Share Count
<p>\$8.6M Cash, Cash Equivalents, and Investments</p>	<p>Cash, Grants, and Access to Capital to Financing Sources to Fund Operations into 2025</p>	<p>\$17.6M CPRIT, with \$6.9M forecast in 2024</p> <p>NIH Funding rGBM through Phase 2 trial</p>	<p>4.5M Basic Common Shares</p> <p>0.14M Series U Warrants (Sept 2024)</p>

Upcoming Key Milestones

LM Cancer Program & ReSPECT-LM Trial

- + Complete Phase 1 single dose trial and present data with at SNO Nov 2024
- + Determine RP2D for Phase 2 single dose trial
- + Initiate Phase 1 multidose trial
- + Evaluate the combination of Rhenium ^{186}Re Obisbameda with PDL1 and PD1 therapies for LM in preclinical models

Brain Parenchymal Cancer Program & ReSPECT-GBM Trial

- + Complete Phase 2 single dose trial and present interim data at SNO Nov 2024
- + Finalize pivotal trial design

Pediatric Brain Cancer Program & ReSPECT-PBC Trial

- + IND approval and initiate enrollment

CSF Diagnostic Program & FORESEE Trial




- + Report FORESEE LM CSF clinical trial data in mid-2024



THANK YOU!

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