

A photograph of a woman with a shaved head and a young girl hugging each other. The woman is on the left, and the girl is on the right. They are both smiling and looking towards each other. The background is a plain, light-colored wall. On the left side of the image, there is a graphic element consisting of a white horizontal line with a white dot at its left end, and a dark blue vertical bar with an orange horizontal bar crossing it.

**Power and precision**  
in cancer radiotherapeutics

**PLUS**<sup>TM</sup>  
THERAPEUTICS

**HCW Healthcare Conference**  
September 14, 2022

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# Forward-Looking Statements

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

Risks & uncertainties for Plus include, but are not limited to: an inability or delay in obtaining required regulatory approvals for product candidates, which may result in unexpected cost expenditures; risks inherent in drug development in general; uncertainties in obtaining successful clinical results for product candidates & unexpected costs that may result therefrom; failure to realize any value of certain product candidates developed & being developed in light of inherent risks & difficulties involved in successfully bringing product candidates to market; inability to develop new product candidates & support existing products; the approval by the FDA & any other similar foreign regulatory authorities of other competing or superior products brought to market; risks resulting from unforeseen side effects; risk that the market for the combined company’s products may not be as large as expected; inability to obtain, maintain & enforce patents & other intellectual property rights or the unexpected costs associated with such enforcement or litigation; inability to obtain & maintain commercial manufacturing arrangements with third-party manufacturers or establish commercial scale manufacturing capabilities; loss of or diminished demand from one or more key customers or distributors; unexpected cost increases & pricing pressures; economic recession & its negative impact on customers, vendors or suppliers; uncertainties of cash flows, expenses & inability to meet working capital needs; & other risks & uncertainties detailed in the risk factors section of Plus’ Form 10-K & Forms 10-Q filed with the SEC, as well as other filings Plus makes with the SEC from time-to-time. Many of these factors that will determine actual results are beyond Plus’ ability to control or predict. Plus disclaims any obligation to update information contained in these forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.



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- + **Texas-Based, Clinical-Stage Targeted Radiotherapeutic Company**  
(Nasdaq: PSTV)
- + **Recent Transactions**
  - + Azaya (2017): nanoliposome tech, facility, team
  - + NanoTx (2020): radiotherapeutic platform
  - + UT San Antonio (2021): microsphere tech
- + **Rare CNS Cancer Clinical Trials**
  - + ReSPECT-GBM: recurrent glioblastoma
  - + ReSPECT-LM: leptomeningeal metastases
- + **Grant Awards**
  - + \$3 Million NIH (GBM through Phase 2)
  - + \$17.6 Million CPRIT (LM through Phase 2)

# Rare & Difficult-to-Treat Cancers

## Responsible for Substantial Morbidity & Mortality Worldwide

- + Rare cancers represent 27% of all cancers; all pediatric cancers are rare
- + Rare cancers account for 25% of all cancer deaths; 5-year survival rate is lower for patients with a rare cancer than those with a more common cancer
- + Treatments for rare cancers are eligible for orphan drug designations

## Central Nervous System Tumors



**Glioblastoma:** deadliest, most common brain cancer in adults (TAM \$2.1B)

**Leptomeningeal Metastases:** late complication in 5% of cancer patients (TAM \$8.4B)

**Pediatric Brain Cancer:** 2<sup>nd</sup> most common type of cancer in children (TAM \$106M)

## Liver Tumors



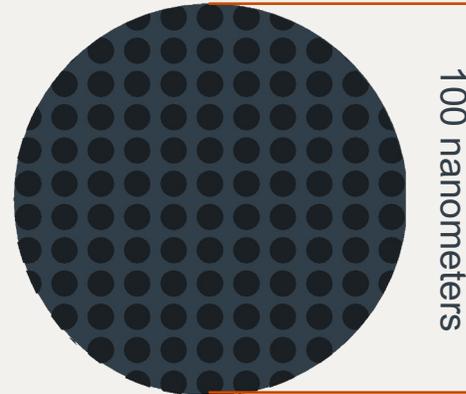
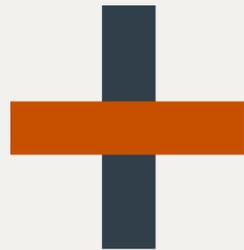
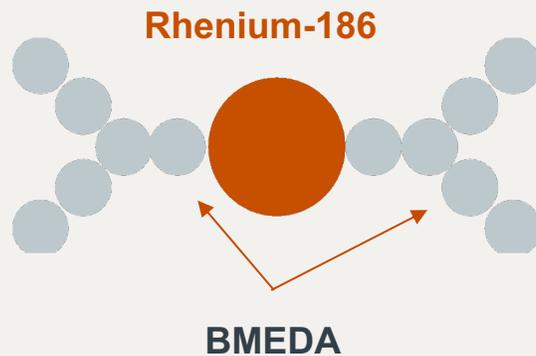
**Hepatocellular Carcinoma:** 42k cases diagnosed annually in U.S. with 5-year survival of 20%

**Colorectal Liver Metastases:** ~50-60% of colorectal cancer patients develop metastases to liver

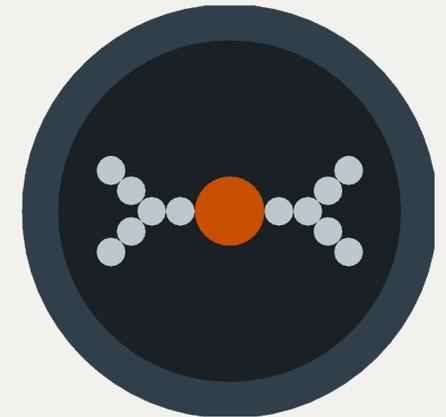
(Combined TAM \$1.3B)

# Lead Investigational Drug: Rhenium-186 NanoLiposome (<sup>186</sup>RNL)

Proprietary Nanoscale Compound  
with a Unique Isotope



NanoLiposome



Rhenium-186  
NanoLiposome

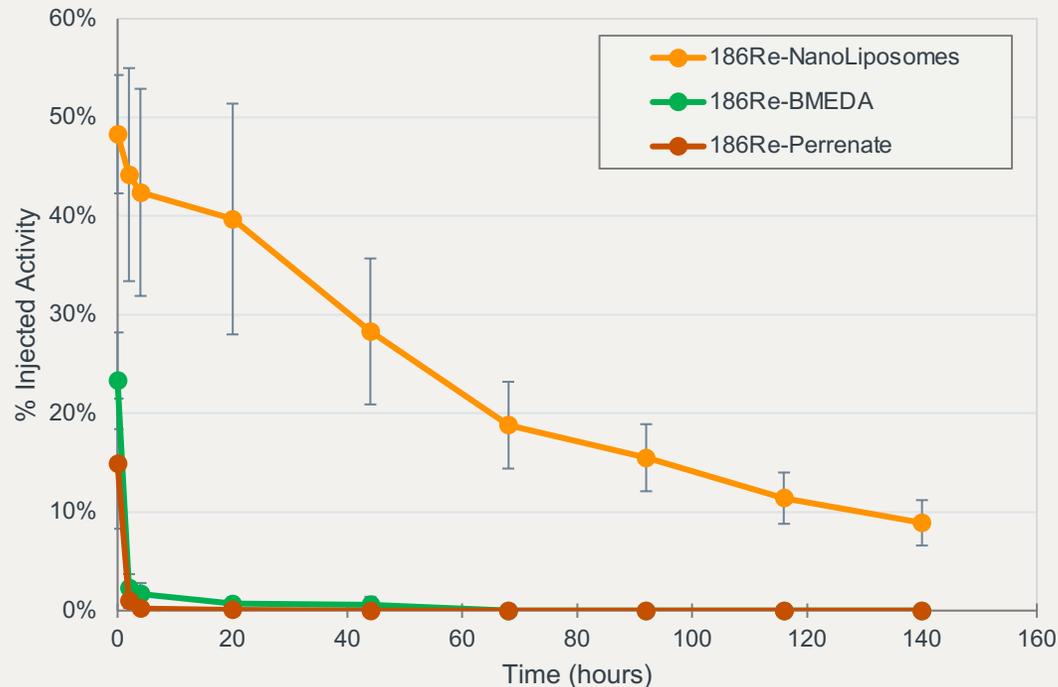
## Rhenium-186 Radioisotope

- + Dual energy emitter: beta (cytotoxic) & gamma (imaging)
- + Short average path length (1.8 mm): high precision
- + Low dose rate: safer for normal tissues
- + High radiation density: overwhelms innate DNA repair mechanisms

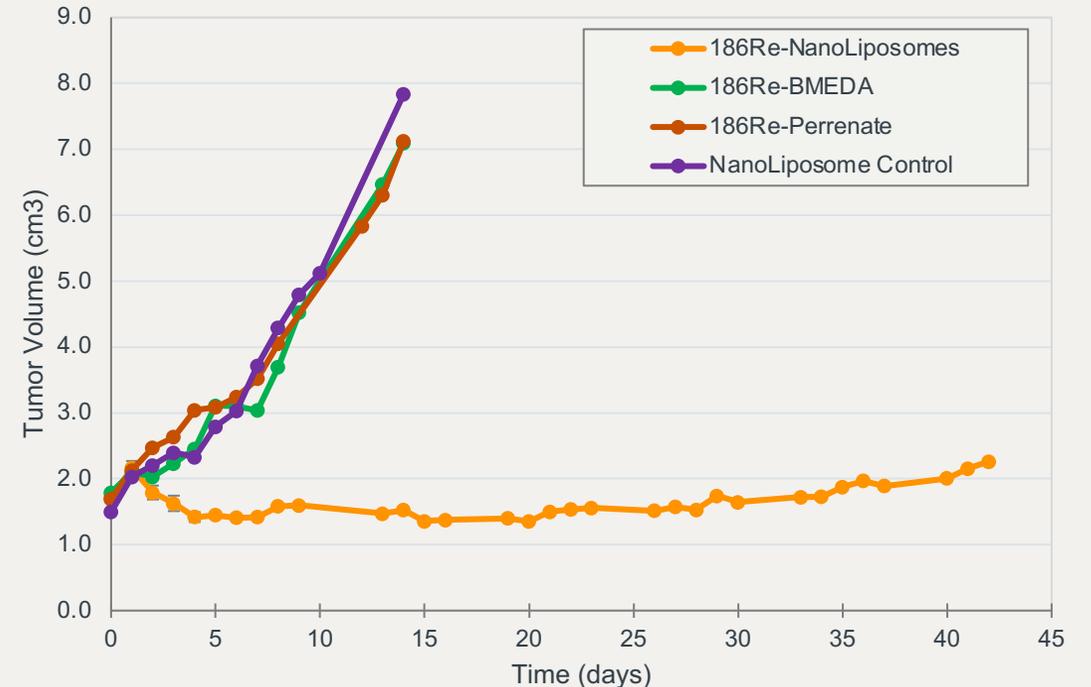
# NanoLiposome Enhances $^{186}\text{Re}$ Tumor Retention & Dispersion

## Resulted in Drastically Reduced Tumor Size & Growth Rate vs. Other Groups

Tumor Retention

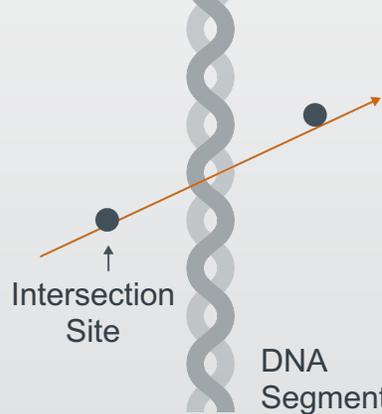
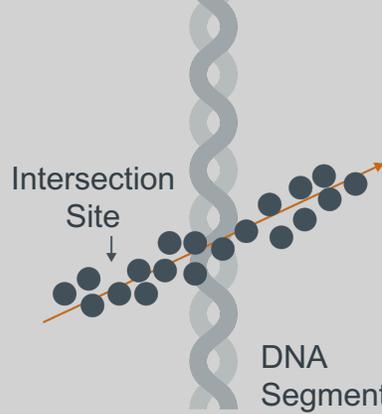


Tumor Response



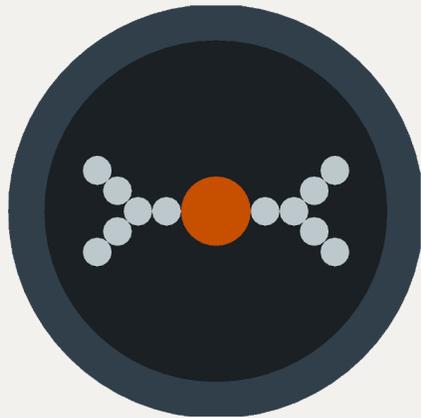
*CED Intratumoral Administration in Head/Neck SCC Xenografts in Nude Rats*

# Targeted, Powerful, & Convenient $^{186}\text{RnL}$ Therapy

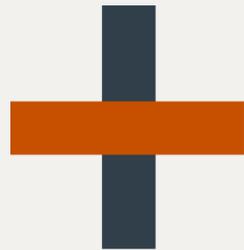
Radiation Types	Total Absorbed Dose	Mechanism of Action	Double-Strand DNA Breaks
 <p data-bbox="254 763 547 806">External Beam</p>	<p data-bbox="802 535 1082 614">35 Gray</p> <p data-bbox="700 621 1184 664">Over Multiple Treatments</p>	 <p data-bbox="1312 671 1490 735">Intersection Site</p> <p data-bbox="1567 735 1694 806">DNA Segment</p>	<p data-bbox="1949 564 2280 635">700-1,400</p>
 <p data-bbox="152 1199 649 1242">Internal Targeted (<math>^{186}\text{RnL}</math>)</p>	<p data-bbox="777 978 1108 1056">600 Gray*</p> <p data-bbox="777 1056 1108 1099">Single Treatment</p>	 <p data-bbox="1312 999 1490 1063">Intersection Site</p> <p data-bbox="1567 1178 1694 1249">DNA Segment</p>	<p data-bbox="1872 1006 2356 1078">12,000-24,000</p>

# Second Investigational Drug: Rhenium-188 NanoLiposome Biodegradable Alginate Microsphere ( $^{188}\text{RNL-BAM}$ )

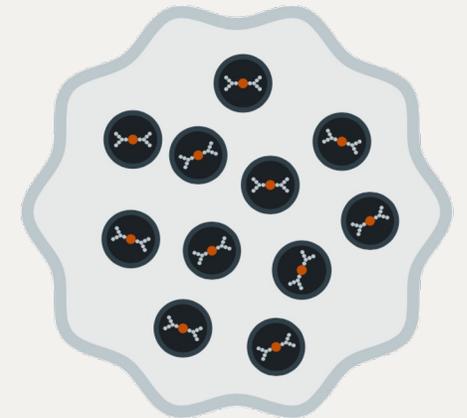
Proprietary Microscale Compound  
with a Unique Isotope



Rhenium-188 NanoLiposome



Biodegradable Alginate Microsphere



Rhenium-188 NanoLiposome  
Biodegradable Alginate Microsphere

## Rhenium-188 Radioisotope

- + Dual energy emitter: beta (cytotoxic) & gamma (imaging)
- + Short average path length (3.1 mm): offers greater precision
- + Low dose rate: safer for normal tissues
- + High radiation density: overwhelms innate DNA repair mechanisms
- + Generator-produced for quick availability

# Pipeline

Investigational Drug	Indication	Administration	FDA Designation	Funding	Stage	Status
<sup>186</sup> RNL Radiotherapeutic	Recurrent Glioblastoma	Intra-tumoral (CED)	+ Orphan Drug + Fast Track	NIH	Phase 1/2a	Enrolling (23 patients to date) Moving into Phase 2 in 2H 2022
	Leptomeningeal Metastases	Intra-ventricular (Ommaya)	Fast Track	CPRIT	Phase 1	Enrolling (4 patients to date)
	Pediatric Brain Cancer	Intra-tumoral (CED)	—	—	Pre-IND	IND Submission 2022
<sup>188</sup> RNL-BAM Radioembolization Therapy	Hepatocellular Carcinoma	Intra-arterial	—	—	Preclinical	IND-Enabling CMC & Preclinical
	Liver Metastases	Intra-arterial	—	—	Preclinical	IND-Enabling CMC & Preclinical



**Innovative, targeted  
radiotherapeutics  
for patients with  
central nervous  
system tumors.**

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# ReSPECT-GBM Phase 1/2 Clinical Trial Design

**Multi-center, sequential cohort, open-label, volume & dose finding study of the safety, tolerability, & distribution of  $^{186}\text{Rn}$  given by convection-enhanced delivery to patients with recurrent or progressive malignant glioma after standard surgical, radiation, and/or chemotherapy treatment.**

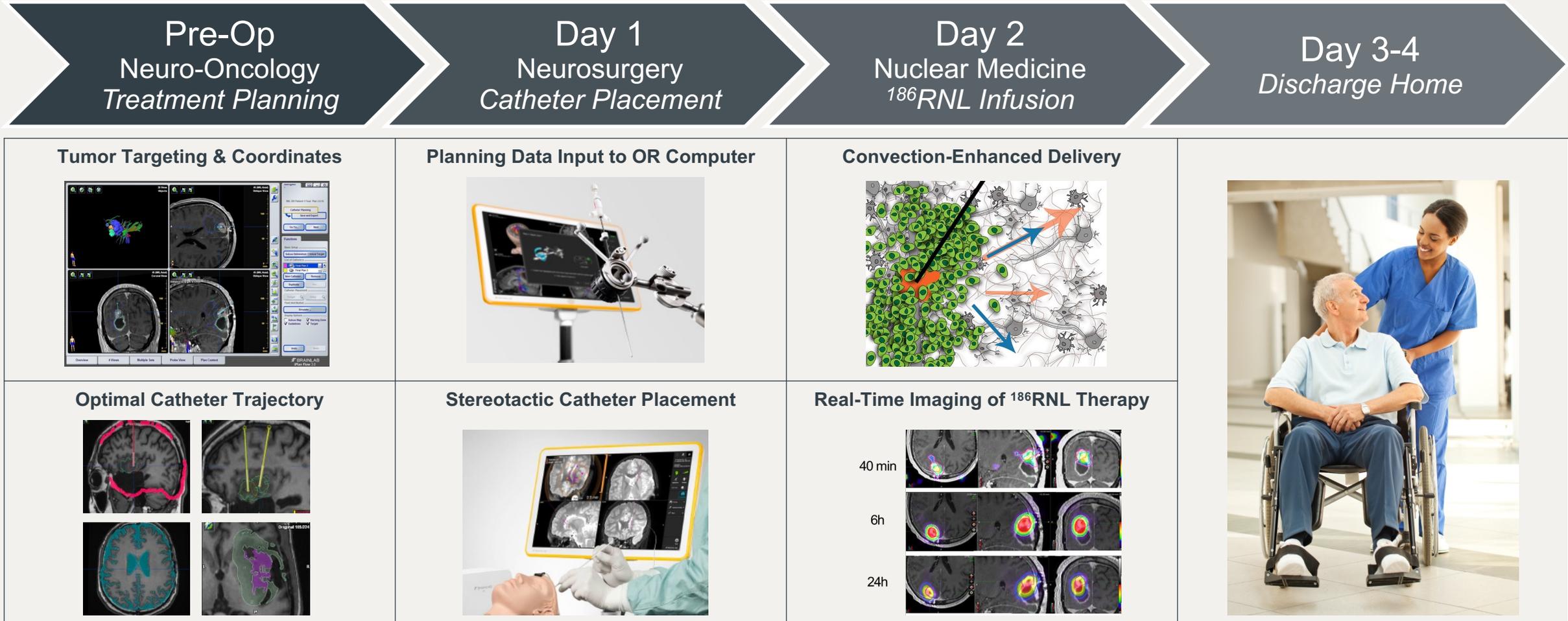
- + Single arm, prospective Phase 1/2 study utilizing a modified Fibonacci dose escalation scheme Phase 1, followed by an expansion at the designated recommended Phase 2 dose (RP2D)
- + Maximum number of subjects: 55
- + Current status: 23 subjects enrolled across 7 dose cohorts at 3 sites
- + Supported by a National Institutes of Health (NIH) grant through Phase 2



*Convection-Enhanced Delivery*



# ReSPECT-GBM Treatment Paradigm



# ReSPECT-GBM Patient Demographics & Dose Escalation

## Patient Demographics (N=23)

Gender	
Male	15 (65%)
Female	8 (35%)
Tumor Volume (cm <sup>3</sup> )	Average = 8.1 Range = 0.9 - 22.8
Prior Treatments	Average = 1.7 Range = 1 - 3
Prior Bevacizumab	5 (22%)
IDH Mutational Status	
Wild type	19 (82%)
Mutated	2 (9%)
Unknown	2 (9%)
MGMT Status	
Methylated	4 (17%)
Unmethylated	12 (52%)
Unknown	7 (30%)
Glioma grade	
Grade IV	21 (91%)
Grade III	2 (9%)

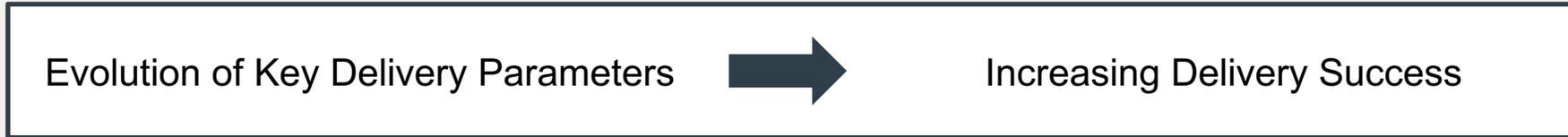
## Dose Escalation

Cohort	Infused Volume (mL)	Total <sup>186</sup> RNL Activity (mCi)	Concentration (mCi/mL)	Average Absorbed Dose (Gy)	Status
1	0.66	1.0	1.5	198	Enrolling Cohort 7 (n=23 subjects)
2	1.32	2.0	1.5	122	
3	2.64	4.0	1.5	234	
4	5.28	8.0	1.5	171	
5	5.28	13.4	2.5	423	
6a	8.80	22.3	2.5	287	
6b*	8.80	22.3	2.5	584	
7	12.28	31.2	2.5	TBD	
8	16.34	41.5	2.5	TBD	

\* Cohort 6b utilized same volume & dose as Cohort 6a but with increase in maximum flow rate to 20 microliters/minute

# ReSPECT-GBM Convection-Enhanced Delivery Optimization

Led to Higher Volumes & Absorbed Radiation Doses in Recent Cohorts



<b>Activity</b>	1.0 – 31.2 mCi
<b>Volume</b>	0.6 – 12.3 mL
<b>Max Flow Rate</b>	5 – 20 ul/min
<b>CED Catheters</b>	1 – 4 per patient

**Cohort 1-4 (low dose & volume)**  
 + 12 patients treated  
 + 5/12 (42%) >100 Gy

**Cohort 5-7 (high dose & volume)**  
 + 11 patients treated  
 + 9/11 (82%) >100 Gy

# ReSPECT-GBM Safety Results

## <sup>186</sup>RNL Appears to be Safe & Well Tolerated

Thus far, in the Phase 1 study of 23 subjects in 8 dosing cohorts with recurrent glioblastoma receiving a single dose of <sup>186</sup>RNL:

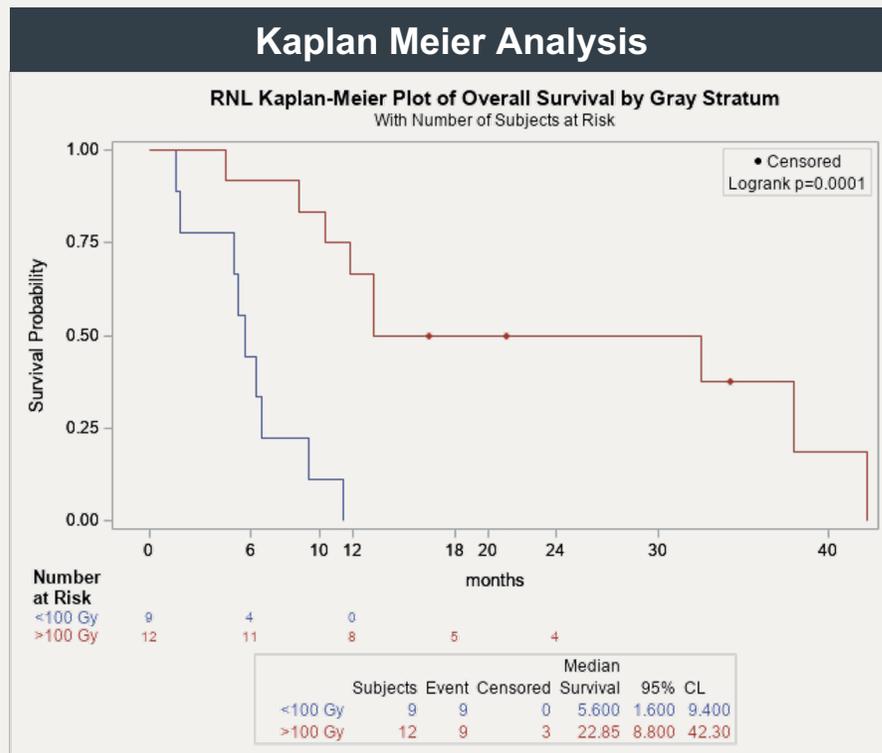
- + There have been no dose limiting toxicities.
- + Most AEs reported were mild or moderate (Grade 1 or 2) in intensity.
- + Most AEs were considered causally unrelated to <sup>186</sup>RNL except scalp discomfort, which was considered related to the surgical procedure.
- + Serious adverse events:

Serious Adverse Event	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Total
Osteonecrosis (Left Shoulder)	0	0	1	0	0	1
Seizure	0	1	2	0	0	3
Vasogenic cerebral edema	0	0	2	0	0	2
Pneumonia	0	0	1	0	0	1

# ReSPECT-GBM Efficacy Results

Statistically Significant Overall Survival Benefit in Therapeutic Doses >100 Gy

## Kaplan Meier Analysis

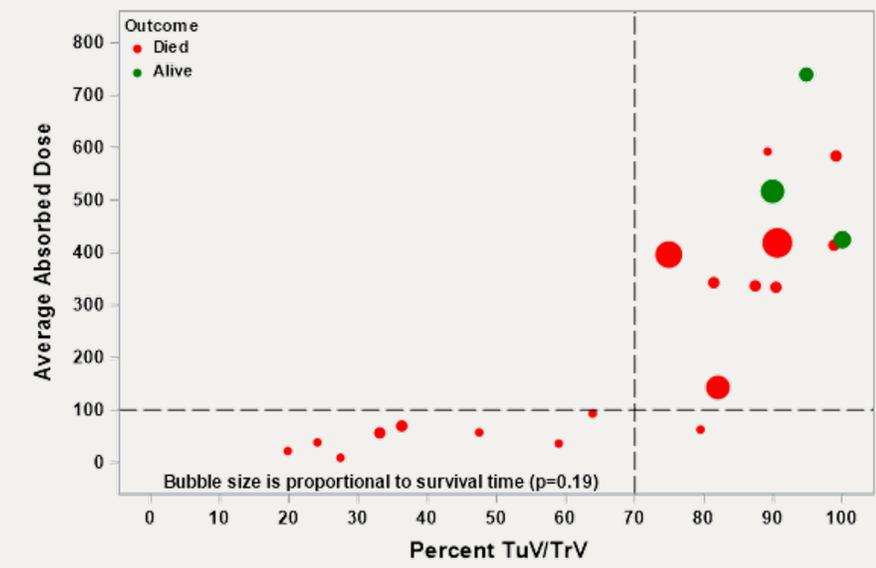


## Overall Survival, N=23

Dose	Median OS (months)	95% CI
All	9.4	5.8, 13.2
<100 Gy	5.6	1.6, 9.4
>100 Gy	22.9	8.8, 42.3

By comparison, **median overall survival of 8 months (32.1 weeks)** reported in 8 study meta-analysis of 694 recurrent GBM patients treated with bevacizumab monotherapy

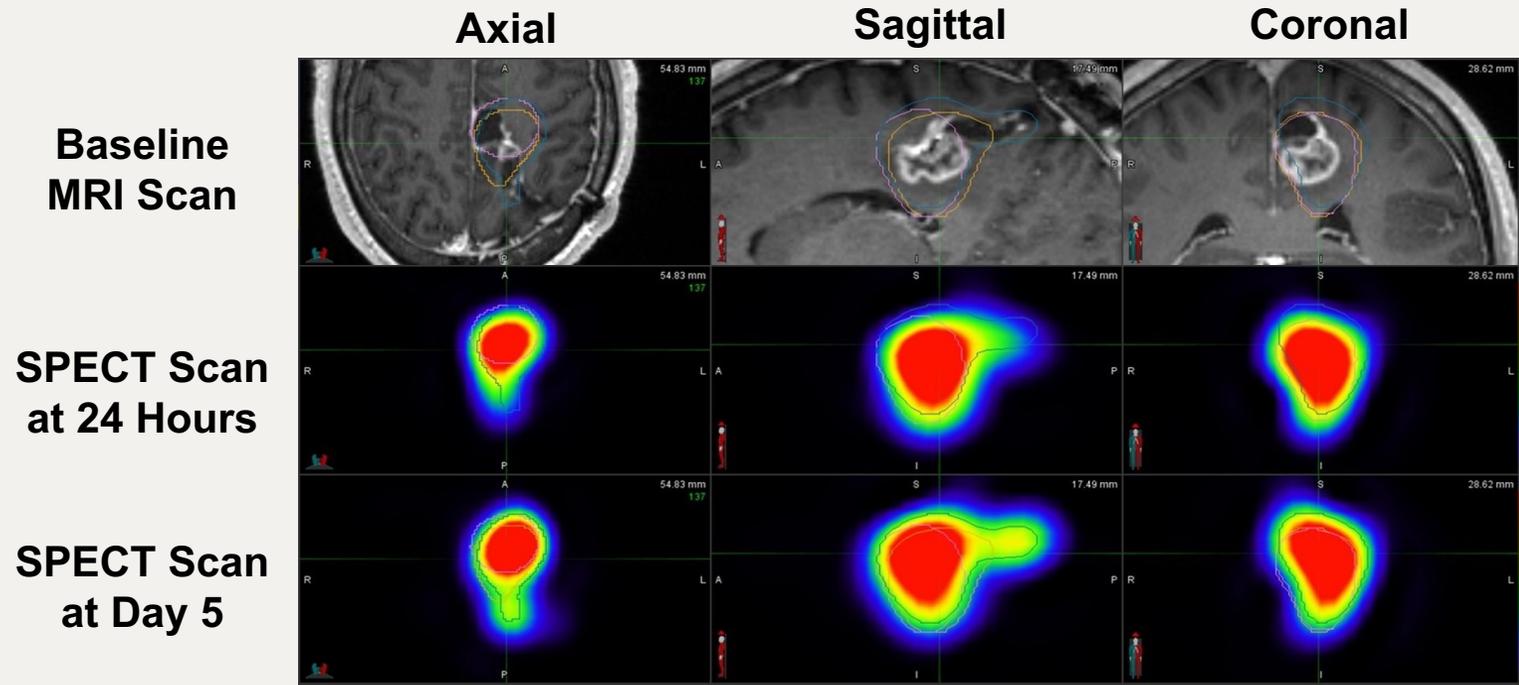
## Therapeutic Threshold >100 Gy



**# Patients Remain Alive**  
>100 Gy - 3 patients  
< 100 Gy - none

# ReSPECT-GBM Case Study: Tumor Coverage & Retention

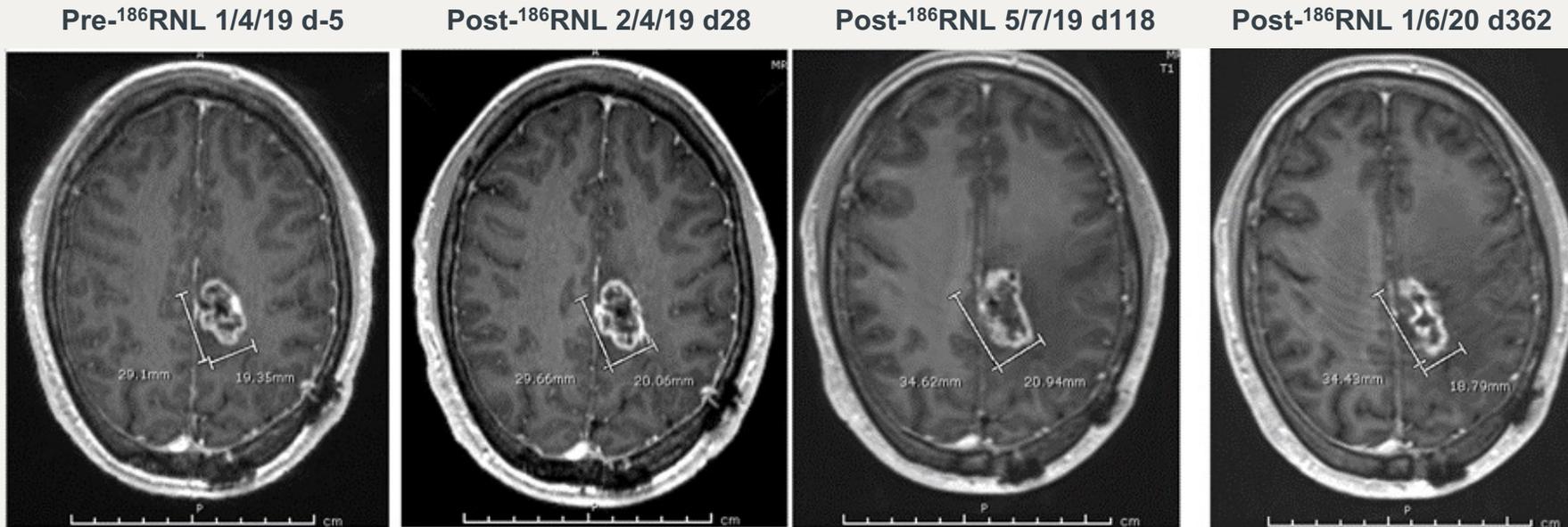
Cohort 5 / Subject 01-014: MRI & SPECT / Radiation Dosimetry



- + Deep brain tumor recurrence
- + Tumor volume: 6.5 mL
- + Tumor coverage: >90%
- + Absorbed dose delivered to tumor: 419 Gy

# Natural History of Recurrent GBM Lesions After $^{186}\text{Rn}$

Cohort 5 / Subject 01-014: Tumor Response Observed to Day 362



- + MRI scans revealed an initial increase in size which peaked at Day 118, with some associated edema, pseudo-progression
- + Tumor shrinkage out to at least Day 362
- + Remains alive at 160 weeks after single treatment

# ReSPECT-LM Phase 1 Clinical Trial Design

A two-part, multi-center Phase 1 study to determine the maximum tolerated dose/ maximum feasible dose, safety, & efficacy of single dose Rhenium-186 NanoLiposome ( $^{186}\text{RNL}$ ) administered via the intraventricular route for leptomeningeal metastases (LM).

## Primary Objective

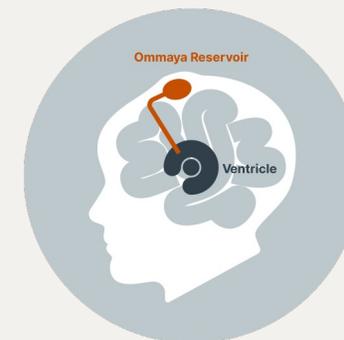
Safety & tolerability of a single dose of  $^{186}\text{RNL}$  by the intraventricular route & to identify a MTD &/or MFD

## Secondary Objectives

- + PK & dosimetry profile of a single dose of  $^{186}\text{RNL}$  when administered intraventricularly via Ommaya reservoir
- + Develop a multiple dosing strategy of  $^{186}\text{RNL}$  for subsequent clinical trials
- + Overall Response Rate (ORR)
- + Duration of Response (DoR)
- + Progression-Free Survival (PFS)
- + Overall Survival (OS)

## Primary Endpoints

- + Incidence & severity of adverse events (AE) & serious adverse events (SAE)
- + Incidence of dose limiting toxicities (DLT)



*Delivery via Ommaya Reservoir*



# ReSPECT-LM Patient Demographics & Dose Escalation

Gender	
Male	2 (50%)
Female	2 (50%)

Primary Tumor	
SCC Right Oropharynx	1 (25%)
Triple Negative Breast	2 (50%)
Lung Adenocarcinoma	1 (50%)

Cohort	Infused Volume (mL)	Total <sup>186</sup> RNL Activity (mCi)	Concentration (mCi/mL)	Theoretical Maximum Absorbed Dose in CSF (Gy)	Status
1	5.0	6.6	1.32	50	Complete (n=3)
2	5.0	13.2	2.64	100	In Progress (n=1)
3	5.0	26.4	5.28	200	Not Started

# ReSPECT-LM Safety Results

## <sup>186</sup>RNL Appears to be Safe & Well Tolerated

- + No treatment-related AEs greater than Grade 1
- + Most common was headache
- + Nonrelated AE's related to SSKI administration

Cohort 1: Subject	Grade 1
02-101	No treatment-related AEs
01-101*	Nausea
	Vomiting
	Headache
	Intermittent Headaches
	Brain Fogginess
01-102	Intermittent Headaches

Cohort 2: Subject	Grade 1
02-102	No treatment-related AEs

# ReSPECT-LM Initial Patient Report

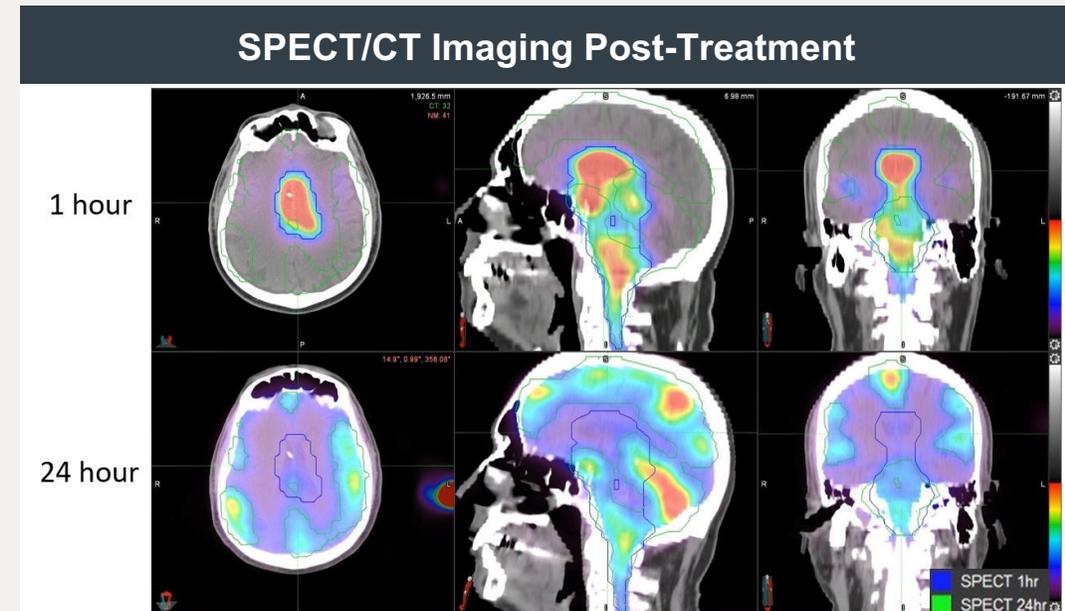
## Cohort 1 / Subject 02-101

70-year-old white male with small cell carcinoma of the right oropharynx with LM of the brain & spinal cord.

Enrolled in Cohort 1 receiving 6.6 mCi  $^{186}\text{Re}$  in 5.0 ml infusate on March 16, 2022.

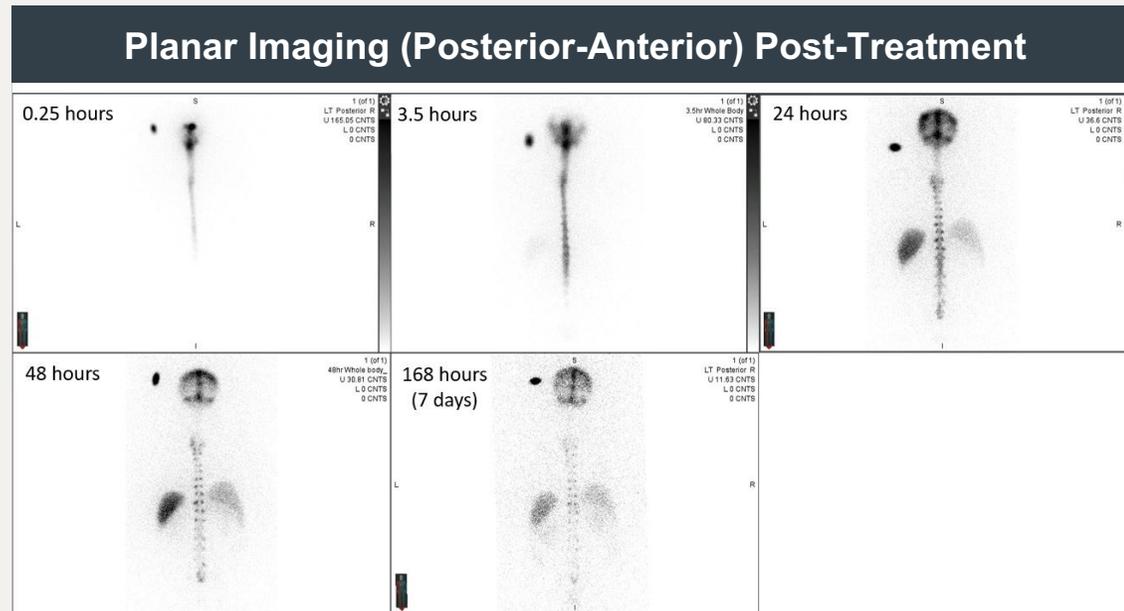
Radiation absorbed dose:

- + Ventricles & cranial subarachnoid space = 29.04 Gy
- + Ventricles (lateral, 3<sup>rd</sup>, & 4<sup>th</sup>) = 14.52 Gy
- + Cranial subarachnoid space = 37.27 Gy
- + Spinal Fluid = 8.97 Gy



# ReSPECT-LM Initial Patient Report

Cohort 1 / Subject 02-101



Assessment	Pre	24 H	48 H	28 D	43 D	56 D
Tumor Cells/mL	70.77	39.79	6.12	7.05	17.11	182.63

The subject was deceased following the last follow-up study visit (death deemed due to progression of primary tumor and not LM), 95 days (13.6 weeks) after enrollment/treatment in the study.

# ReSPECT-LM Initial Patient Report

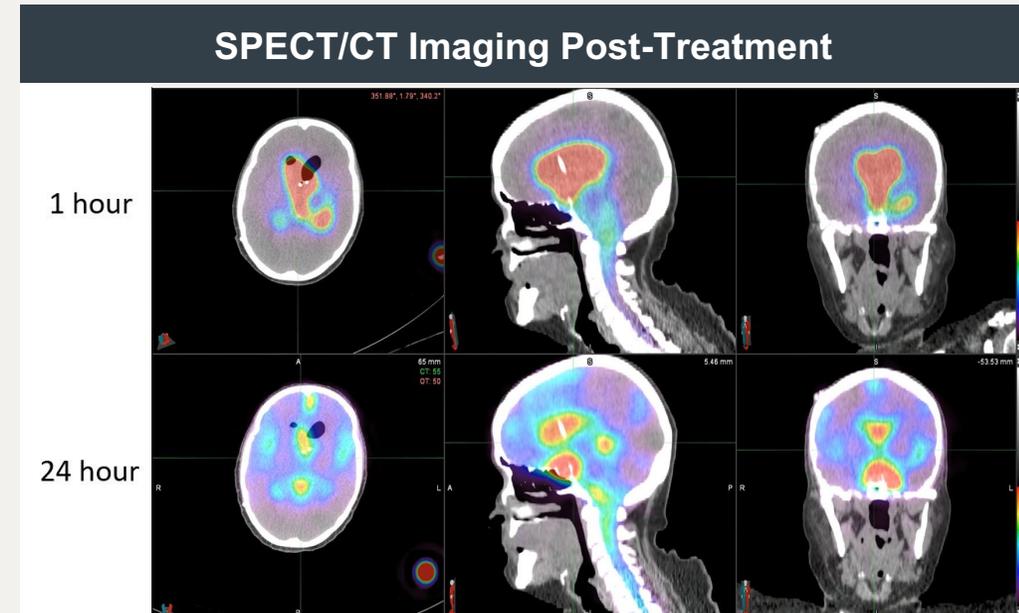
## Cohort 1 / Subject 01-102

60 year old with Stage III Invasive Lobular Breast Carcinoma of the right breast (2016); bone metastases (06/2020), leptomeningeal metastasis (01/2022) with conversion to triple negative within the CSF.

Enrolled in Cohort 1 receiving 6.6 mCi  $^{186}\text{RnL}$  in 5.0 ml infusate on June 15, 2022.

Radiation absorbed dose:

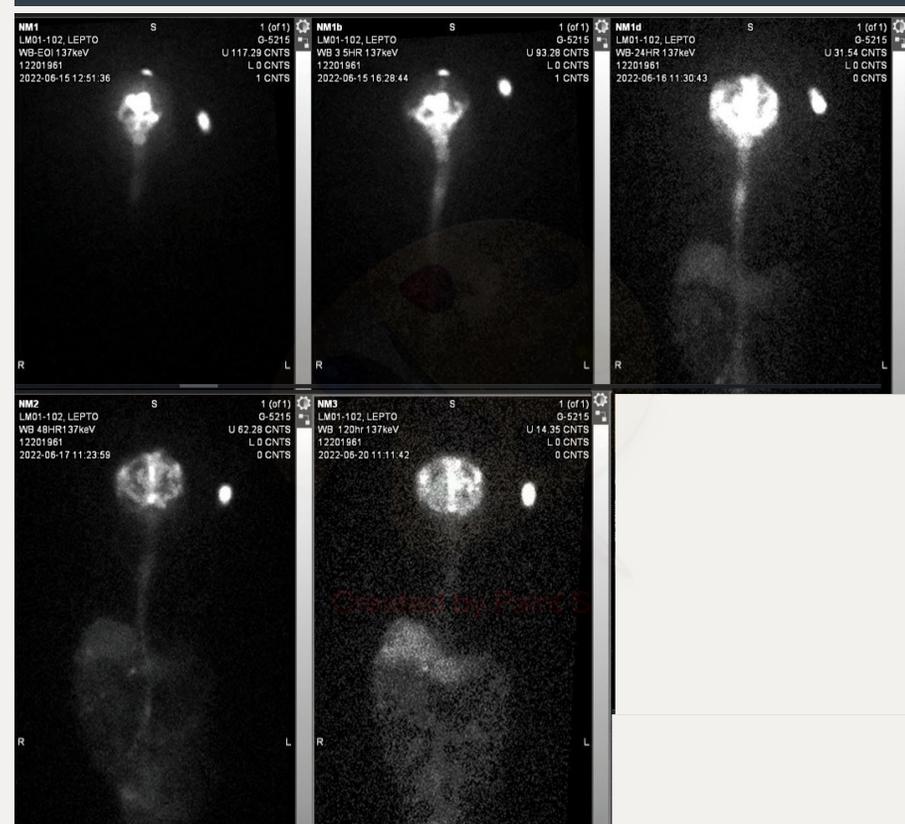
- + Ventricles and cranial subarachnoid space = 26.80 Gy
- + Ventricles (lateral, 3<sup>rd</sup>, & 4<sup>th</sup>) = 36.44 Gy
- + Cranial subarachnoid space = 21.25 Gy
- + Spinal Fluid = 5.76 Gy



# ReSPECT-LM Initial Patient Report

## Cohort 1 / Subject 01-102

### Planar Imaging (Posterior-Anterior) Post-Treatment



Assessment	Pre	24 H	48 H	28 D	56 D
Tumor Cells/mL	839.13	455.29	506.73	395.1	1133

The subject was alive and clinically stable as of the last follow-up at day 39 after enrollment/treatment in the study.

## ReSPECT-LM Summary

- +  $^{186}\text{RnL}$  is a nanoliposomal radiotherapeutic with a short pathlength allowing for a larger therapeutic window & higher safe absorbed doses than conventional radiation
- +  $^{186}\text{RnL}$  is administered through a standard intraventricular catheter, redistributes throughout the CSF, & retains in the leptomeninges through day 7
- + A single administered dose of 6.6 mCi in 5.0 mL (Cohort 1) achieves absorbed doses of 18.7 to 29.0 Gy to the ventricles & cranial subarachnoid space
- + Cohort 2 has commenced, using 13.2 mCi in 5.0 mL; absorbed dose evaluation in progress
- +  $^{186}\text{RnL}$  at 6.6 mCi was well tolerated with no trAEs > Grade 1; Cohort at 13.2 mCi was well tolerated in the first patient without any AEs. Importantly, PI reported improvement in the patient's presenting LM complications of double vision, ataxia, muscle weakness, and lower extremity pain.
- + All 4 patients (3 in Cohort 1, 1 in Cohort 2) experienced a decreased CSF cell count by microfluidic chamber assay after treatment, ranging from ~55 to 92%
- + Dose escalation is continuing & repeated dosing will be explored

**Innovative, targeted  
radiotherapeutics  
for patients with  
liver tumors.**

**PLUS™**  
THERAPEUTICS



# Liver Cancer is the 6<sup>th</sup> Most Common & 3<sup>rd</sup> Deadliest Cancer

TARE is One of Many Locoregional Treatment Modalities Described in NCCN Guidelines

## The Challenges

### Hepatocellular Carcinoma

The most common type of primary liver cancer.

- + Incidence: 42k
- + 5-Year Survival: 20%

### Metastatic Colorectal Cancer

A secondary form of liver cancer with a high level of severity.

- + Incidence: 150K
- + 5-Year Survival: 14%



## The TARE Market

- + Two Yttrium-90 based products available in U.S. for 20+ years
- + Increasingly common treatment option despite lack of conclusive RCT data
- + Moderate growth expected in Asia Pacific due to highest liver cancer incidence
- + High procedure cost limits growth in more financially constrained countries

# <sup>188</sup>RNL-BAM Radioembolization Therapy for Liver Tumors

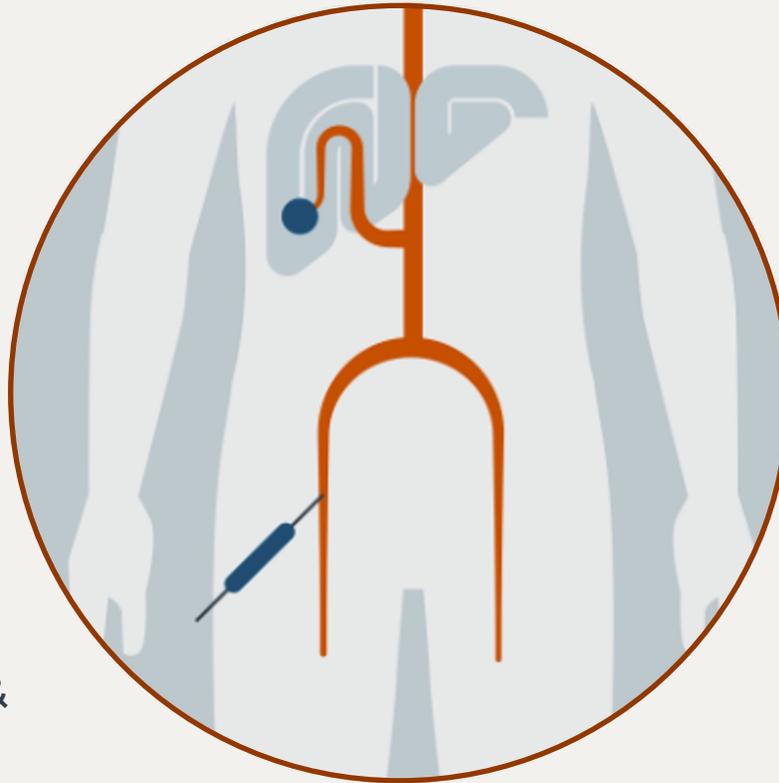
Focused on TARE Product/Clinical Improvement & Global Market Disruption

## The Approach

A single intra-arterial injection of <sup>188</sup>RNL-BAM in which biodegradable microspheres block the blood flow to the targeted solid organ tumors & simultaneously deliver a therapeutic payload of radiation.

## The Opportunities

Extend the life of patients with liver cancer through a safer, more targeted, & convenient treatment approach.



## The Potential Advantages

Compared to 2 radioembolization therapies currently available in U.S., <sup>188</sup>RNL-BAM may offer:

- 1) Work-up predictive of final clinical outcome (same chemistry to label microspheres with <sup>99m</sup>Tc as <sup>188</sup>Re)
- 2) Higher quality imaging (gamma photon)
- 3) Radioactivity retention (nanoliposome)
- 4) Clearance (microsphere degradation)
- 5) Patient access, affordability, convenience (generator produced <sup>188</sup>Re)

# 2022 Corporate Milestones

- + ReSPECT-GBM Phase 2 trial for small to medium tumors
  - + FDA CMC & Clinical Type C meetings - completed
  - + Complete CMC activities for  $^{186}\text{RNL}$  for GMP/registrational drug supply - Q3
  - + Initiate enrollment - 2022
- + ReSPECT-GBM Phase 1 dose escalation for large tumors – 2022 enrolling
- + ReSPECT-GBM  $^{186}\text{RNL}$  multi-dose extension trial – approved & active
- + ReSPECT-LM Phase 1 enrollment of Cohort 2 - ongoing
- + ReSPECT-PBC IND approval & Phase 1 trial initiation for pediatric ependymoma & high-grade glioma
- +  $^{186}\text{RNL}$ -BAM technology transfer & key CMC, FDA IND-enabling studies
- + Complete additional preclinical studies
- + Planned data presentations in H2 2022: ASCO/SNO Brain Mets, ESMO, EANM, SNO

# Capitalization Summary

Select Data as of June 30, 2022	
<b>Cash</b>	\$18.1M
<b>Common Shares Outstanding</b>	22,468,682
<b>Series U warrants</b>	2,141,000