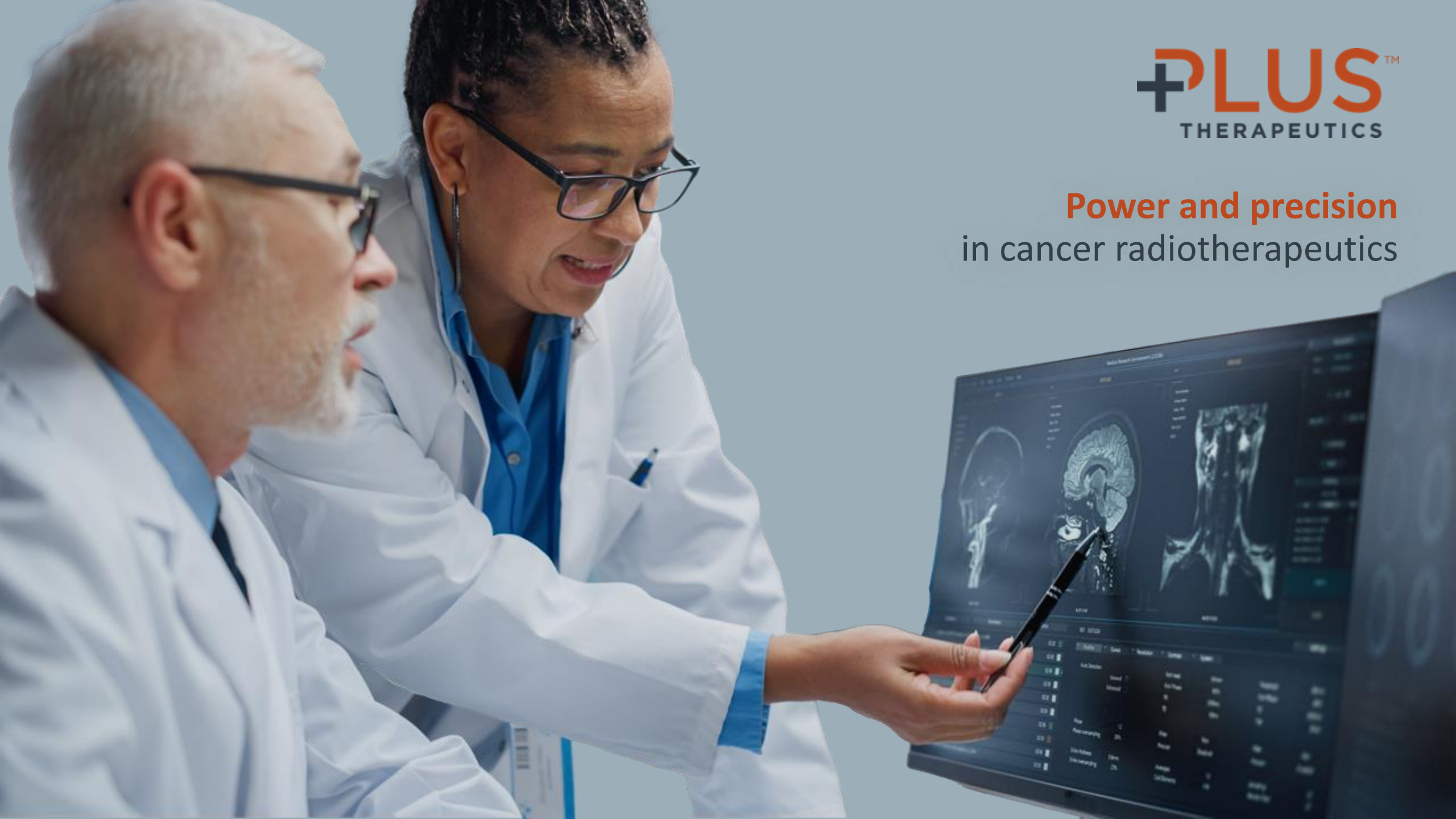
PLUS™ THERAPEUTICS

Power and precision
in cancer radiotherapeutics



Forward Looking Statement

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

Risks & uncertainties for Plus include, but are not limited to: the early stage of Plus’s product candidates and therapies, the results of Plus’s research and development activities, including uncertainties relating to the clinical trials of its product candidates and therapies; Plus’s liquidity and capital resources and its ability to raise additional cash, the outcome of Plus’s partnering/licensing efforts, risks associated with laws or regulatory requirements applicable to it, market conditions, product performance, litigation or potential litigation, and competition within the cancer diagnostics and therapeutics field, among others; and additional risks described under the heading “Risk Factors” in Plus’s Securities and Exchange Commission filings, including in Plus’s annual and quarterly reports. There may be events in the future that Plus is unable to predict, or over which it has no control, and its business, financial condition, results of operations and prospects may change in the future. Plus assumes no responsibility to update or revise any forward-looking statements to reflect events, trends or circumstances after the date they are made unless Plus has an obligation under U.S. federal securities laws to do so.

Clinical Stage, Targeted Radiotherapeutics for Central Nervous System Cancers (CNS)

Publicly listed (Nasdaq: PSTV) based in Texas

Platform Technologies

+ Rhenium radionuclides
+ Proprietary drug loading technology
+ Radiolabeled nano-/micro-carriers
+ Patent protection thru 2041

Ideal for CNS indications

Direct tumor targeting

Mature supply chain & partnerships

CNS Cancer Focus

+ Recurrent glioblastoma, Phase 2
+ Leptomeningeal mets, Phase 1
+ Pediatric brain cancer, Phase 1
+ Next-gen radioembolization therapy

> $15B total addressable market

Significant unmet medical needs

No DLTs & promising efficacy

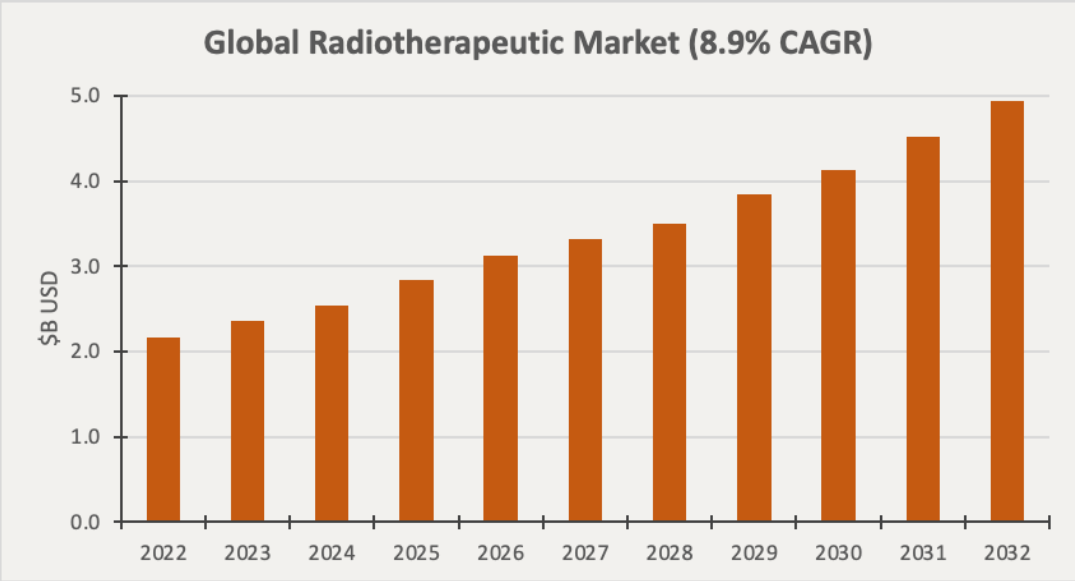
Financial Foundation

+ Capital efficient
+ >$20M grants (NIH, CPRIT)
+ $60M in cash/equity facilities
+ NASDAQ: PSTV highly liquid

Capitalizing PSTV at low cost of capital

Next-Generation Radiotherapeutic Market Landscape

High Growth Expectations Over Next Decade



Future Projected Global Radiotherapeutic Market:

+ Global market is projected to doubling in size in 10 years
+ North America had 47% of the market share in 2022
+ Europe had 39% of the market share in 2022
+ Asia Pacific will grow at the highest CAGR % from 2023-32

Summary of the Radiotherapeutic Market Today:

+ Commercial successes (LUTATHERA, $471M annual sales)
+ Recent FDA approvals (PLUVICTO, $2B+ peak annual sales forecasted)
+ Compelling clinical data (XOFIGO, 3.6 month survival benefit)
+ Significant private/public deal activity – financings, mergers, strategic partnerships
+ Expanding institutional coverage of market & individual companies
+ >50 radiopharmaceutical programs in the clinic; ~20 companies in discovery/preclinical
+ Approved products concentrated in β-emitters for few targets/indications (PSMA/prostate, SSTR/NET)
+ 2nd gen PSMA-targeted radiotherapeutics in development to address 1st gen deficiencies
+ Continued radioisotope supply & drug production challenges

Source: market.us report on radiopharmaceutical market April 2023

PLUS Pursuing >$15B Addressable Cancer Market Opportunity

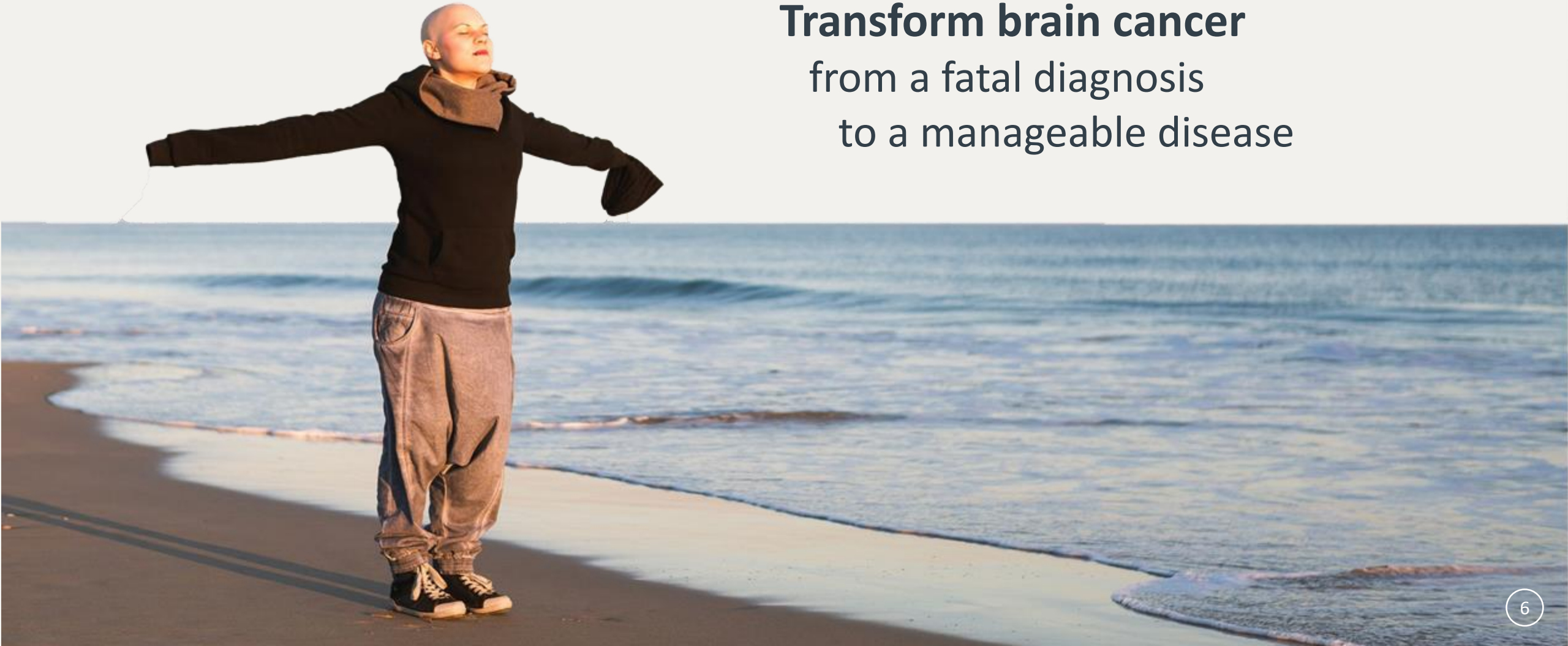
Radiotherapeutic platform is expandable beyond CNS to solid tumors

	Indication	U.S. Incidence	Standard of Care: Median Overall Survival	5-Year Survival Rate	Total Addressable Market
CNS	**Recurrent Glioblastoma (GBM)**	14,500	8 months	7%	$2.1B
CNS	**Pediatric Ependymoma**	250	Variable	75%	$100M
CNS	**Pediatric High-Grade Glioma (HGG)**	800	14-20 months	<20%	
CNS	**Leptomeningeal Metastases from Solid Tumors (LM)**	155,000	3-9 months	<3%	$8.4B
Solid Tumors	**Primary & Secondary Liver Cancer**	190,000	6-10 months	21-44%	$1.3B
Solid Tumors	**Other Indications**	~500,000	Variable	Variable	$3B

Rhenium Re^{186} Obisbemeda has been evaluated in published preclinical studies for **breast cancer, head/neck cancer & peritoneal carcinomatosis**

~2 month improvement is clinically meaningful & potentially approvable by FDA

Our Goal



Transform brain cancer
from a fatal diagnosis
to a manageable disease

First to Market Radiopharmaceuticals for CNS Cancers

PLUS direct targeted delivery of CNS radiotherapeutics is the best approach

Good



External Beam Radiation Therapy

+ Standard of care
+ Requires fractionation
+ Limited absorbed dose
+ Limited by off-target toxicity

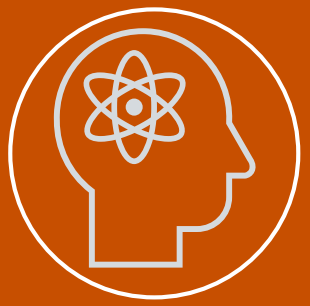
Better



Molecular Targeted Radiation Therapy

+ Reliant on receptor specificity
+ Delivered systemically
+ Few cross BBB
+ Off-target toxicity

Best



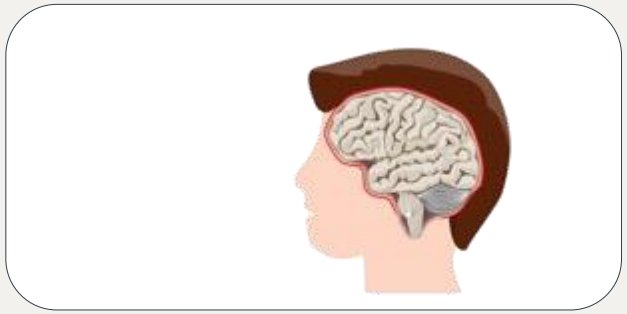
Direct Targeted Delivery

+ Direct delivery to the tumor site
+ BBB challenge eliminated
+ Minimal off-target effects
+ Can quantify absorbed dose
+ Safe delivery of high doses

PLUS Direct Targeted Drug Delivery Strategies for CNS Cancers

Overcomes the primary 'barrier' to CNS drug development

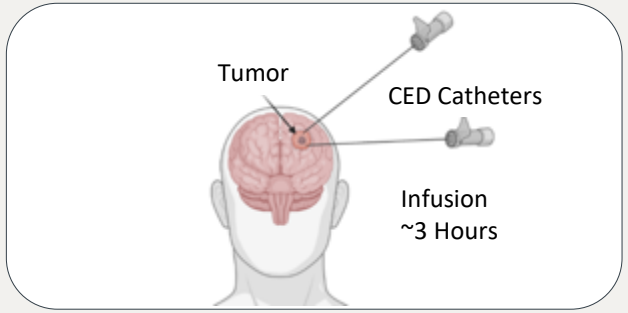
Blood-Brain-Barrier (BBB)



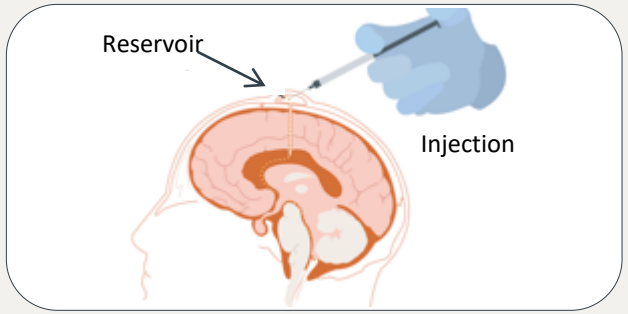
CNS Drug Delivery Limitations

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

Brain Parenchyma



Cerebrospinal Fluid



Convection-Enhanced Delivery (CED)

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

Ommaya Reservoir

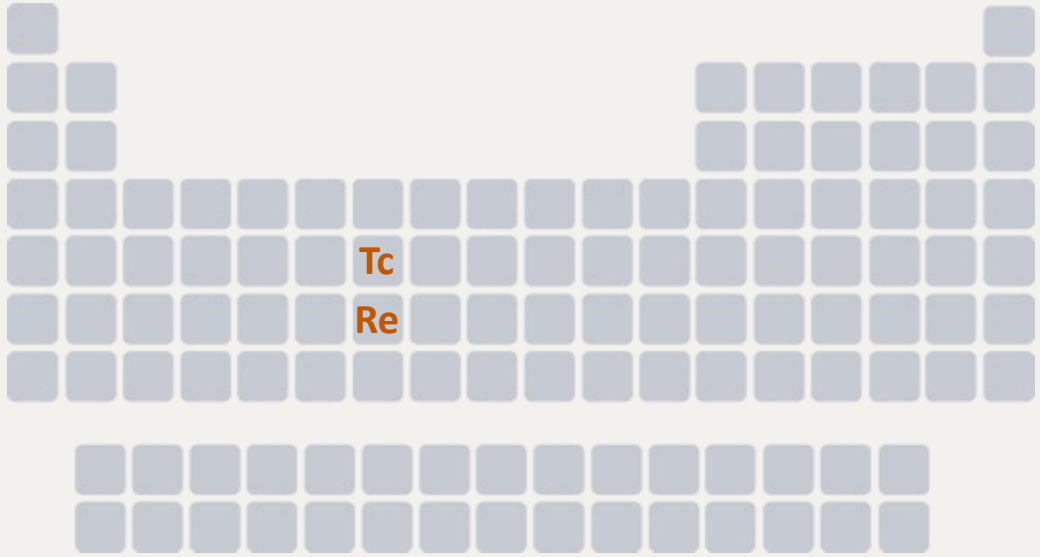
+ FDA-approved and utilized for 60+ years
+ Bypasses BBB
+ Small reservoir is placed under the scalp and allows drug to be directly delivered to the ventricle
+ Allows multi-drug dosing and CSF sampling
+ Commonly placed in LM patients

PLUS Uses Isotopic Rhenium for CNS Indications

Ideal radioisotope for CNS tumors

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

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



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

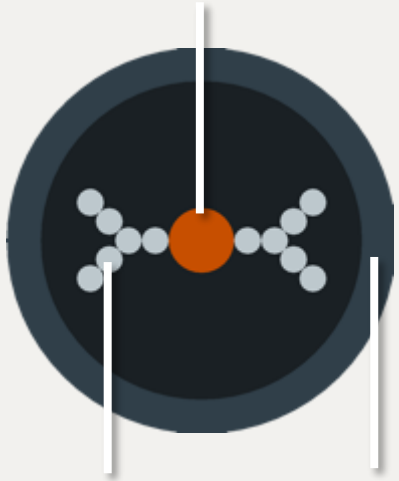
PLUS' Lead Drug Rhenium Re^{186} Obisbemeda Prolongs Radiation in the Brain & CSF

Complementary technologies drive efficacy & safety profile

Rhenium Re^{186} Obisbemeda

Rhenium-186 Radionuclide

Emits tumor destroying radiation over short distances while sparing healthy tissue



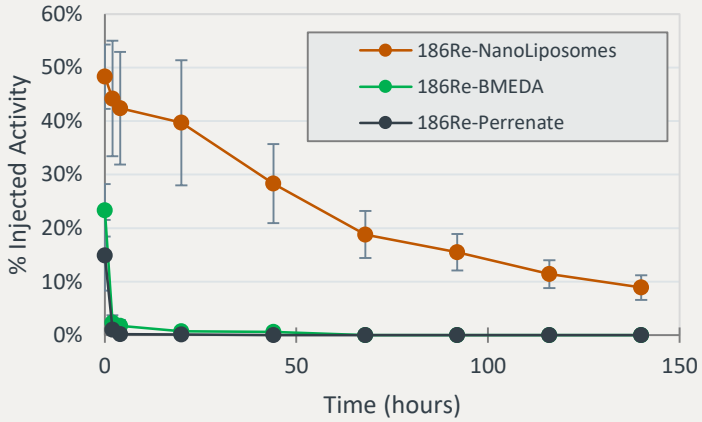
BMEDA Small Molecule

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

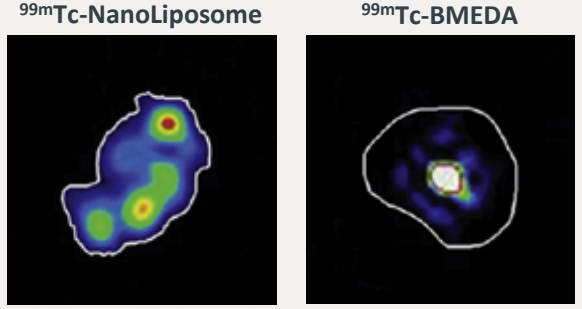
100 nm NanoLiposome

Carries BMEDA-Rhenium to target tumor & improves retention

Tumor Retention



Improved Drug Distribution Coverage

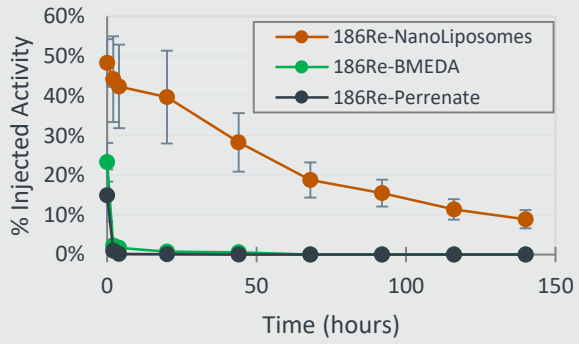


Sources: Phillips, W. et al. *Advanced Drug Delivery Reviews,* 2014

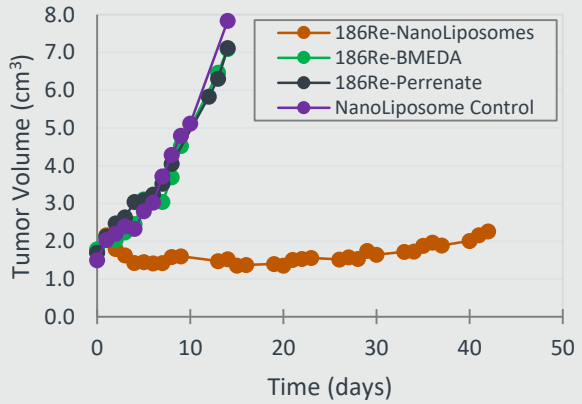
Preclinical Evidence for Rhenium Re^{186} Obisbemeda Use in CNS Cancers

Nanoliposome Enhances Tumor Dispersion & Response

Tumor Retention

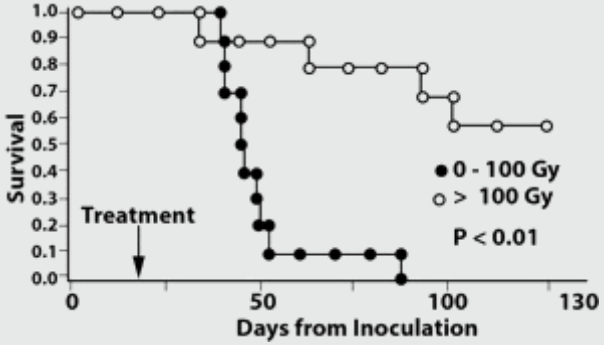


Tumor Response



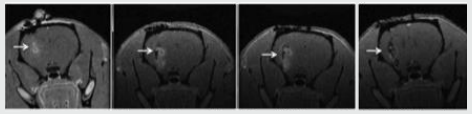
Glioblastoma Intracranial Xenograft Model

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

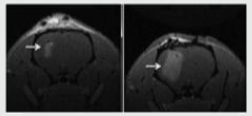


^{186}Re Treated Tumors Progressively Disappear Over Time

186Re-Liposome Treatment

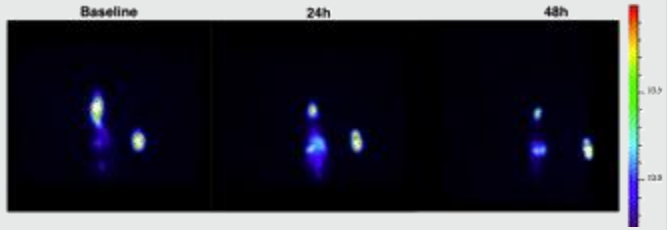


Control

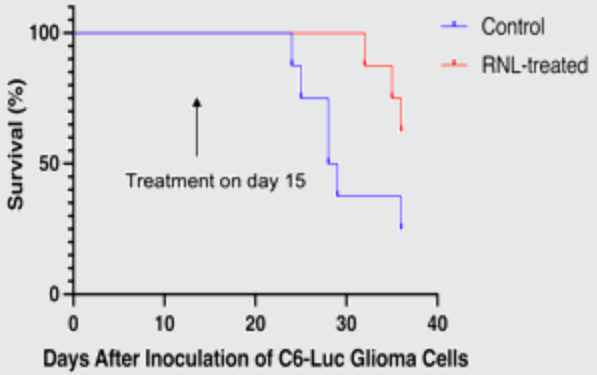


Leptomeningeal Metastases Wistar Rat Model

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



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

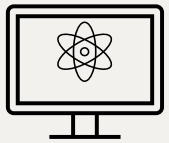


Sources: Phillips, W. et al. *Advanced Drug Delivery Reviews,* 2014; Phillips, W. et al. *Neuro-Oncology*, 2012; Balinda, H. et al. *SNO Brain Metastases Meeting,* 2021

PLUS' Technology Provides Better Patient Experience for CNS Cancer Care

Radiotherapy in a short inpatient hospitalization or single outpatient visit

Personalized Treatment Planning → SoC Biopsy & Catheter Placement → Drug Infusion → Patient Monitoring






Indication	Week Prior to Treatment	Day 1	Day 2	Day 3
• **Recurrent GBM** • **Ped Ependymoma** • **Ped HGG**	MRI imaging to assess & plan catheter number, trajectory & flow rate	Standard of care biopsy followed by catheter placement in OR	Single ~4-hour infusion & real-time imaging in hospital Nuclear Medicine department	Catheter removal & patient discharged
Leptomeningeal Metastases	CSF flow study to confirm no flow obstruction	Single 5-minute injection in outpatient setting		

Rhenium Re^{186} Obisbemeda Supply Chain

Strategic partnerships ensure long-term cGMP drug supply through commercialization

	Target Irradiation	*Isotope Production*	*cGMP Intermediate Manufacture*	*cGMP Chelator*	*Critical Raw Materials & Components*	*Drug Manufacturing & Dose Prep*	*Last-Mile Delivery*
	Irradiation Services	**Critical Material Supply**	**Intermediate Manufacturing**	**Critical Material Supply**	**Critical Material Supply**	**Drug Product Manufacturing**	**Shipping Logistics**
Rhenium Re^{186} Obisbemeda	**Rhenium-186** + Exclusive supply of cGMP Re-186 + Alternate suppliers under evaluation MURR	**Rhenium-186** + Exclusive supply of cGMP Re-186 IsoTherapeutics Group, LLC	**Gradient Liposome** + 5-year Master Supply Agreement for Manufacturing of cGMP Liposome intermediate Piramal Pharma Solutions	**BMEDA** + 10-year supply exclusivity for cGMP BMEDA ABX	+ Supply agreement pending + >1 year inventory PALL REPLIGEN Avanti Polar Lipids, Inc.	+ 5-year Master Supply Agreement for cGMP Manufacturing + Alternate: Alamo Nuclear RadioMedix	+ Nationwide: MNX + Texas: Alamo Nuclear MNX Global Logistics Alamo Nuclear Pharmacy
Rhenium Re^{188} Nanoliposome Biodegradable Alginate Microsphere	**Rhenium-188** + Isotope provided as a Tungsten-188 Generator + Supply Agreement pending ONCOBETA	**Rhenium-188** + Supply agreement pending RadioMedix	**Alginate Microsphere** + Additional suppliers under evaluation + Pending finalizing formulation and manufacturing process	**BMEDA** + 10-year supply exclusivity for cGMP BMEDA ABX	+ Additional suppliers under evaluation + Pending finalizing formulation and manufacturing process Avanti Polar Lipids, Inc.	+ 5-year Master Supply Agreement for Manufacturing + Preclinical & Phase 1 Supply Alamo Nuclear Pharmacy	+ Texas: Alamo Nuclear Alamo Nuclear Pharmacy

PLUS Drug Development Pipeline

Substantial pipeline expansion continues through 2023

Theranostic: Rhenium Re^{186} Obisbemeda		Preclinical	IND	Phase 1	Phase 2
Malignant Gliomas	Recurrent Glioblastoma (large tumors)	**ReSPECT-GBM Phase 1**			
	Recurrent Glioblastoma (small-medium tumors)	**ReSPECT-GBM Phase 2**			
	Pediatric Ependymoma	**ReSPECT-PBC Phase 1/2**			
	Pediatric High-Grade Glioma				
Leptomeningeal Metastases	Various Solid Tumors	**ReSPECT-LM Phase 1 / Part A Complete**			
	Breast Cancer			**Phase 1 / Part B**	
	Lung Cancer				
	Melanoma	**ReSPECT-LM**			

Theranostic: Rhenium Re^{188} NanoLiposome Biodegradable Alginate Microsphere		Preclinical	IND	Phase 1	Phase 2
Various Solid Tumors	Primary & Secondary Liver Cancer				
	Other				



Leptomeningeal Metastases

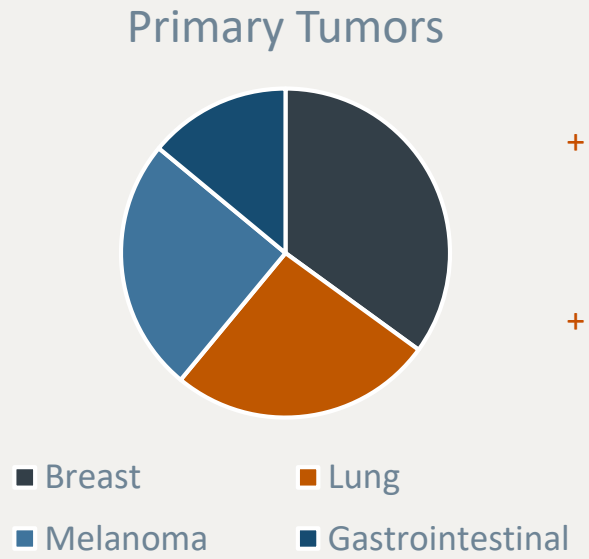
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Leptomeningeal Metastases: Disease & Market Assessment

A late-stage cancer complication with a poor prognosis & no FDA-approved treatments

Overview

- Dismal survival of 4-6 weeks without treatment
- Increasing incidence with ~155,000 U.S. patients per year
- Likely 2-4x underdiagnosed based on autopsy findings
  - **3-8%** of solid tumor patients will be diagnosed with LM during illness course
  - **20%** of cancer patients demonstrated LM at autopsy
  - **40%** of patients positive for LM at autopsy had negative CSF cytology prior to death
- No standard of care but treatments (systemic therapy for primary cancer & neuroaxis-directed chemo & radiation) but treatments may relieve symptoms, but do not halt disease progression or impact survival



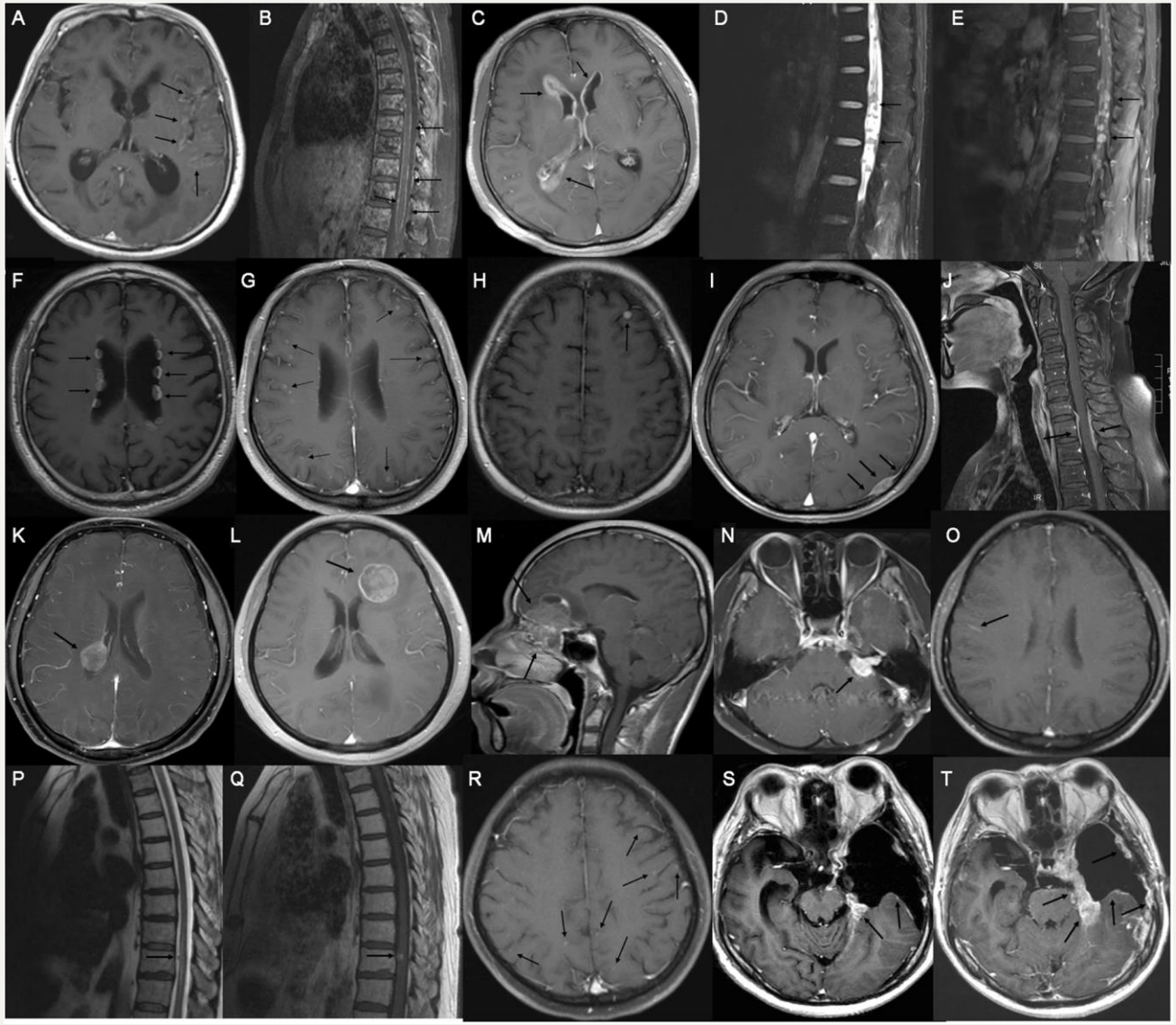
- Breast, lung, melanoma, and GI main primary cancers for LM
- Additional opportunities to treat brain, CUP, and hematological cancers

Opportunity

Treat LM with a first-in-class radiotherapeutic that provides more targeted dose in a single administration versus traditional radiation therapy.

Jayson GC Cancer 1994; 74:3135-41.
Lee JL J Neurooncol 2004; 66:167-74
Smith DB. Eur JSurg Oncol 1985; 11:36-6.
Weitzner MA. Cancer 1995; 76:1804-8.
Ongerboer de Visser BW. Neurology 1983; 33:1565-72.
Posner JB Neurologic complications of cancer, F.A. Davis, Phil. 1995.
Shapiro WR Cancer Treat Rep. 1977;61(4):733.
Posner JB Adv Neurol. 1978;19:579.

Imaging & Leptomeningeal Metastases

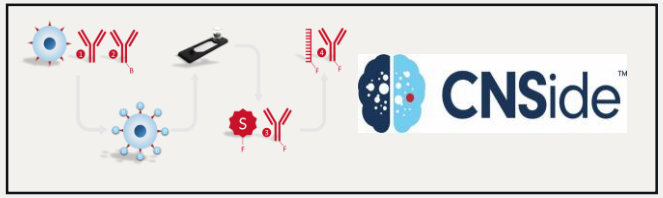


(A) Diffuse pial enhancement in brain sulcus, especially the left temporal lobe.
(**B**) Diffuse leptomeningeal enhancement in vertebral canal.
(**C**) Enhancement of subependyma in the bilateral ventricles.
(**D**) Multiple nodular lesions in spinal canal in T2-weighted sequences.
(**E**) Obvious enhancement in contrast enhanced T1-weighted sequences.
(**F**) Multiple nodular lesions with enhancement in the wall of lateral ventricles.
(**G**) Enhancement of metastatic nodules in cerebral cortex.
(**H**) Metastatic lesion in subarachnoid space.
(I) Dural enhancement in left occiput and rat-tail sign were observed.
(**J**) Dural enhancement in local spinal canal.
(**K**) Metastatic lesion in the posterior horn of the right lateral ventricle.
(**L**) Metastatic lesion correlated to the anterior horn of the left lateral ventricle.
(**M**) The rhabdomyosarcoma of paranasal sinus and nasal cavity invaded across the bottom of anterior cranial fossa and the frontal lobe.
(**N**) The enhancement of auditory and facial nerves at the left cerebellopontine angle.
(**O**) Fuzzy pial enhancement presented at the sulcus and gyrus.
(**P**,**Q**) A Lesion of implantation metastasis on the surface of spinal cord.
(**R**) The occult metastatic nodules in cerebral cortex.
(**S**) Subdural hydroma at the left tempus. Slight enhancement of the local dura mater.
(**T**) One month later, it showed worse subdural effusion and diffusely dural thickening and enhancement.

Diagnosis and Treatment of LM with Rhenium 186 Obisbemeda

LM Diagnosis Difficult

- **Clinical presentation**
  - 50% patients may have neurologic symptoms
  - Inconsistent, non-localized, non-specific symptoms
- **Imaging**
  - Not sensitive to early involvement or treatment changes
  - Nonspecific
- **CSF cytology**
  - Traditional cytology lacks sensitivity and specificity
  - ***New CSF cell testing technology CNSide tumor cell enumeration technology (Biocept):***
    - ***92% sensitive***
    - ***100% specific***

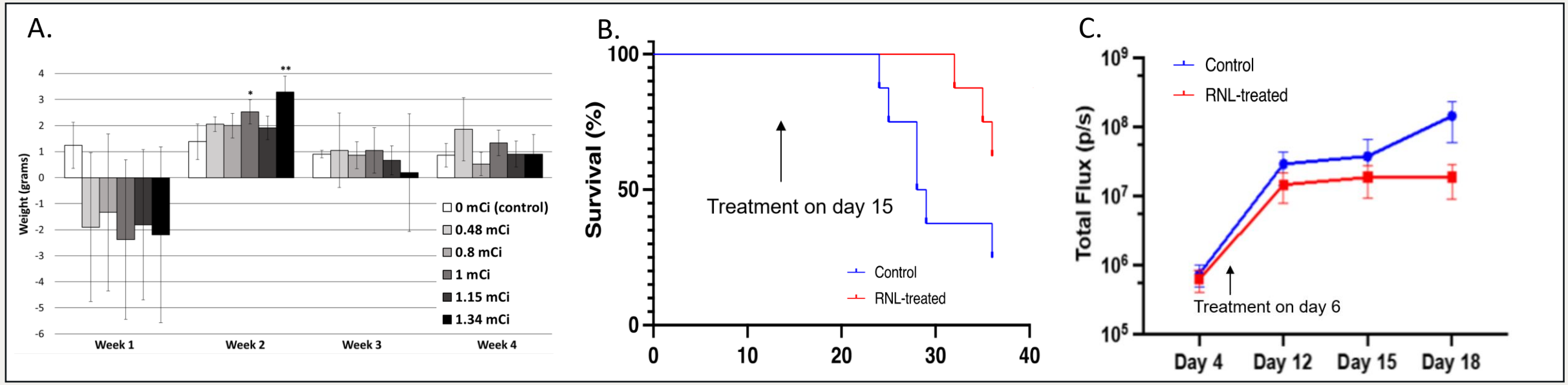


Why Rhenium 186 Obisbemeda?

- Rhenium-186 is an ideal radionuclide for CNS indications: long half-life (~90 hours), short path length (~2mm), low dose rate and high radiation density
- Liposomal encapsulation has been shown to prolong retention in the brain and CSF (e.g., DepoCyt®)
- Uptake by tumor associated macrophages
- ^{186}RNL should deliver high absorbed doses of radiation to disease within the leptomeningeal space while significantly limiting off target effects (brain, spinal cord, white matter, bone marrow)

^{186}RNL Preclinical Science: Retention, Tumor Coverage, Efficacy, Safety

- SAFETY- Preclinical evaluation of ^{186}RNL by intraventricular injection in non-tumor bearing rats with up to 1.34 mCi with corresponding absorbed doses of 1,075Gy was without significant toxicity. The only significant histologic finding among treated rats was thickening of the leptomeninges overlying the median eminence suggesting a mild reactive meningeal hypertrophy
- EFFICACY- In 2 LM models (Wistar/C6 and NSG/MDA-MB-231) treatment with ^{186}RNL resulted in prolonged survival.



A. Weight post RNL in non-tumor bearing Wistar rats.
B. Survival curve for animals with intrathecal C6 treated with blank (blue) or RNL (red).
C. Bioluminescence of LM MDA-MB-231 in nude rats treated with blank (blue) or RNL (red)

ReSPECT-LM U.S. Phase 1/2 Clinical Trial

Multicenter, Phase 1 dose-escalation study to establish the safety and tolerability of a single dose of ^{186}RNL by the intraventricular route (via Ommaya reservoir).

Study Design

- 2 Part Phase 1 design (Part A cohorts 1-3 and Part B cohorts 4+)
- Primary objective is to determine a maximum tolerated dose (MTD) and/or maximum feasible dose (MFD).
- The study utilizes a modified 3+3 design. Dose Level (DL) 1 in the first cohort based on the results of the preclinical pharmacokinetic/biodistribution/dosimetry and toxicology studies.
- Starting dose is up to 6.6 mCi as a single dose with a target absorbed dose of maximal possible dose of 50 Gy or less.
- Dose doubling for the first three cohorts, followed by a safety review prior to cohort 4.
- Expansion cohorts for Breast (n=20) and NSCLC (n=20)
- Phase 1 Part A Dose Escalation:

Cohort	Infused Volume (mL)	Activity (mCi)	Concentration (mCi/mL)	Theoretical Max Absorbed Dose (Gy)	Increase (%)
1	5	6.6	1.32	50	N/A
2	5	13.2	2.64	100	100
3	5	26.4	5.28	200	100

ReSPECT-LM U.S. Phase 1A Clinical Trial

Inclusion & Exclusion Criteria

Inclusion Criteria

1) Subject has proven and documented LM that meets the requirements for the study:
   - EANO-ESMO Clinical Practice Guidelines Type 1 and 2 (with the exception of 2D) **LM of any primary type**.
   - Karnofsky performance status of 60 to 100
   - Standard organ function requirements

Exclusion Criteria

1) Obstructive or symptomatic communicating hydrocephalus
2) Ventriculo-peritoneal or ventriculo-atrial shunts without programable valves or contraindications to placement of Ommaya reservoir
3) Patients who had any dose to the spinal cord or whole brain radiation therapy, regardless of when the radiation treatment was delivered.
4) Standard concomitant illness restrictions

ReSPECT-LM Phase 1 Clinical Trial Endpoints

ReSPECT™ CLINICAL TRIALS

Cancer Prevention & Research Institute of Texas

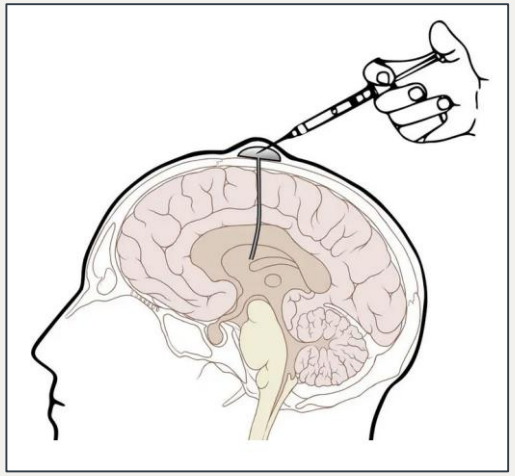
A two-part, multi-center Phase 1 study to determine the maximum tolerated dose/maximum feasible dose, safety, & efficacy of single dose Rhenium (186Re) obisbemeda administered via the intraventricular route for leptomeningeal metastases (LM).

Primary Objective

Safety & tolerability of a single dose of Rhenium (^{186}Re) obisbemeda by the intraventricular route & to identify a MTD &/or MFD

Secondary Objectives

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



Delivery via Ommaya Reservoir

UT Health San Antonio

UT Southwestern Medical Center®

Northwestern Medicine®

Primary Endpoints

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

ClinicalTrials.gov: NCT05034497

ReSPECT-LM U.S. Phase 1 Clinical Trial Imaging & CSF Sampling

Post-Procedure Imaging and CSF Sampling

Assessment	Day 1	Day 2	Day 3	Day 7
Whole Body Planar	EOI* and EOI+3.5 hours	EOI+24 hours (± 6 hours)	EOI+48 hours (± 6 hours)	EOI+96 hours (± 2 days)
SPECT/CT	EOI+30 minutes (after WBP)	EOI+24 hours (± 6 hours)		

Assessment	Day 1	Day 2	Day 3
CSF for PK and Activity	5 hours post dose (± 20 minutes)	24 hours post dose (± 2 hours)	48 hours post dose (± 2 hours)

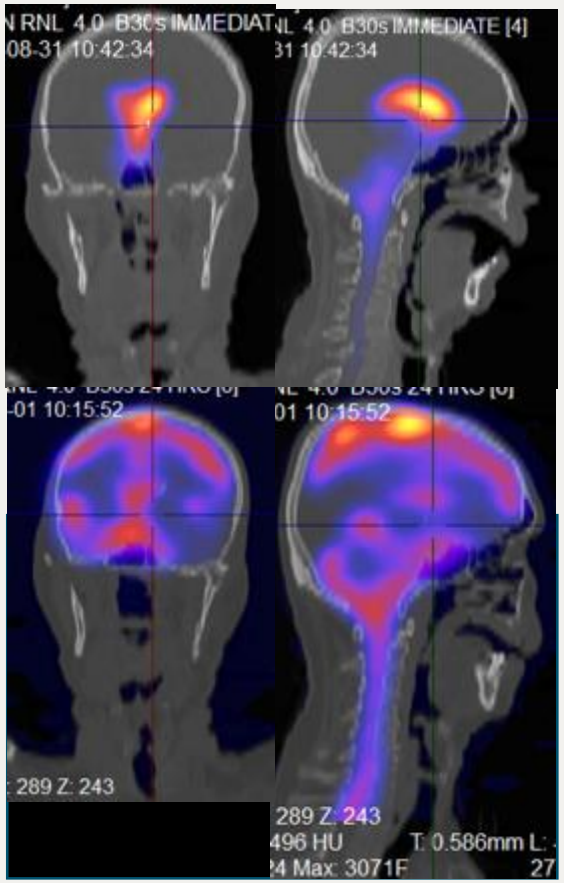
* End of Infusion

ReSPECT-LM for Leptomeningeal Metastases

Real-time imaging shows rapid diffusion in CSF space

Immediate

24 hours





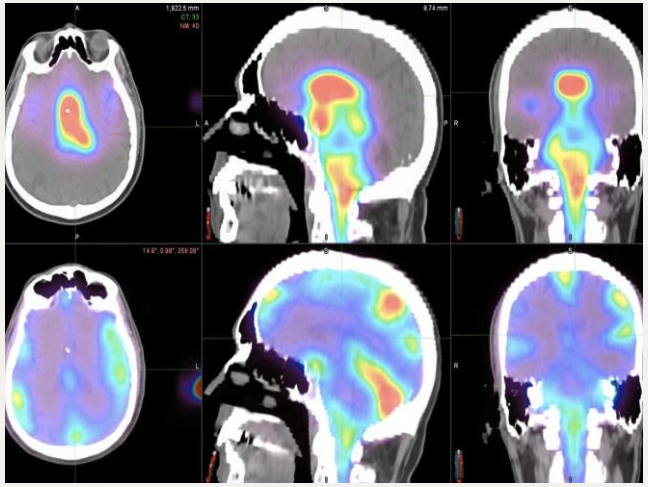


ReSPECT-LM Phase 1 Clinical Trial – Dose Escalation

Patient 02-101

- 70 year old white male
- **Small cell carcinoma of the right oropharynx** with metastases in the brain (Oligodendroglioma) and spinal cord, identified leptomeningeal disease on 12 February 2022
- Enrolled in **Cohort 1** and treated with 6.6 mCi ^{186}RNL in 5.0 ml infusate on 16 March 2022

Region	Radiation Absorbed Dose (Gy)
Ventricles and cranial subarachnoid space	29.04
Ventricles (lateral, 3rd, and 4th)	14.52
Cranial subarachnoid space	37.27
Spinal Fluid	8.97

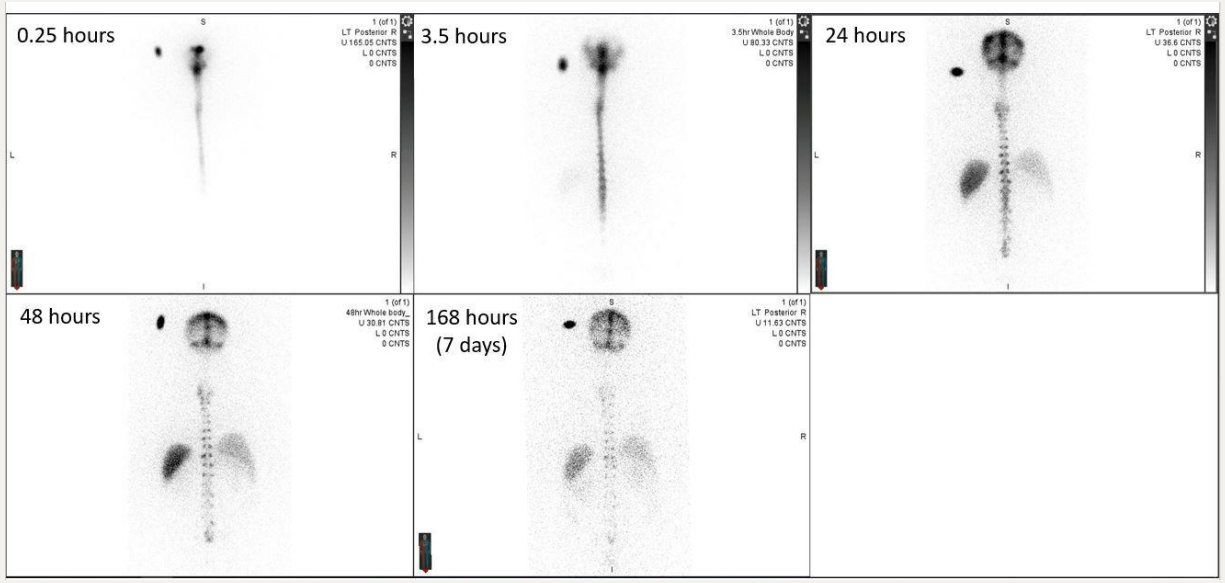


ReSPECT-LM Phase 1 Clinical Trial – Dose Escalation

Mays Cancer Center

Patient 02-101

Planar Imaging (Posterior-Anterior) Post-Treatment



Assessment: Tumor Cells/mL

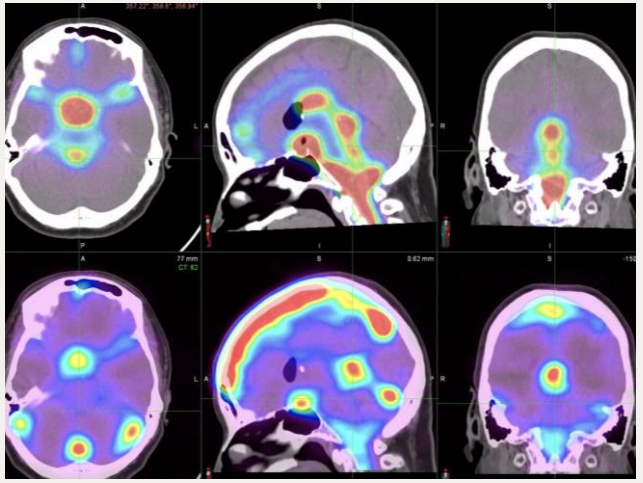
Pre	5 hrs	24 hrs	48 hrs	14 days	28 days	43 days	56 days
70.77	8.33	39.79	6.12	6.45	7.05	17.11	182.63

ReSPECT-LM Phase 1 Clinical Trial – Dose Escalation

Patient 01-101

- 59 year old white female
- Cancer right upper quadrant diagnosis in 1998; **metastatic breast cancer** with unspecified estrogen receptor status (right HCC) diagnosis on 09 April 2018; leptomeningeal carcinomatosis, chest wall and regional lymph node metastases from her breast cancer on 02 November 2018
- Enrolled in **Cohort 1** and treated with 6.6 mCi ^{186}RNL in 5.0 ml infusate on 27 April 2022

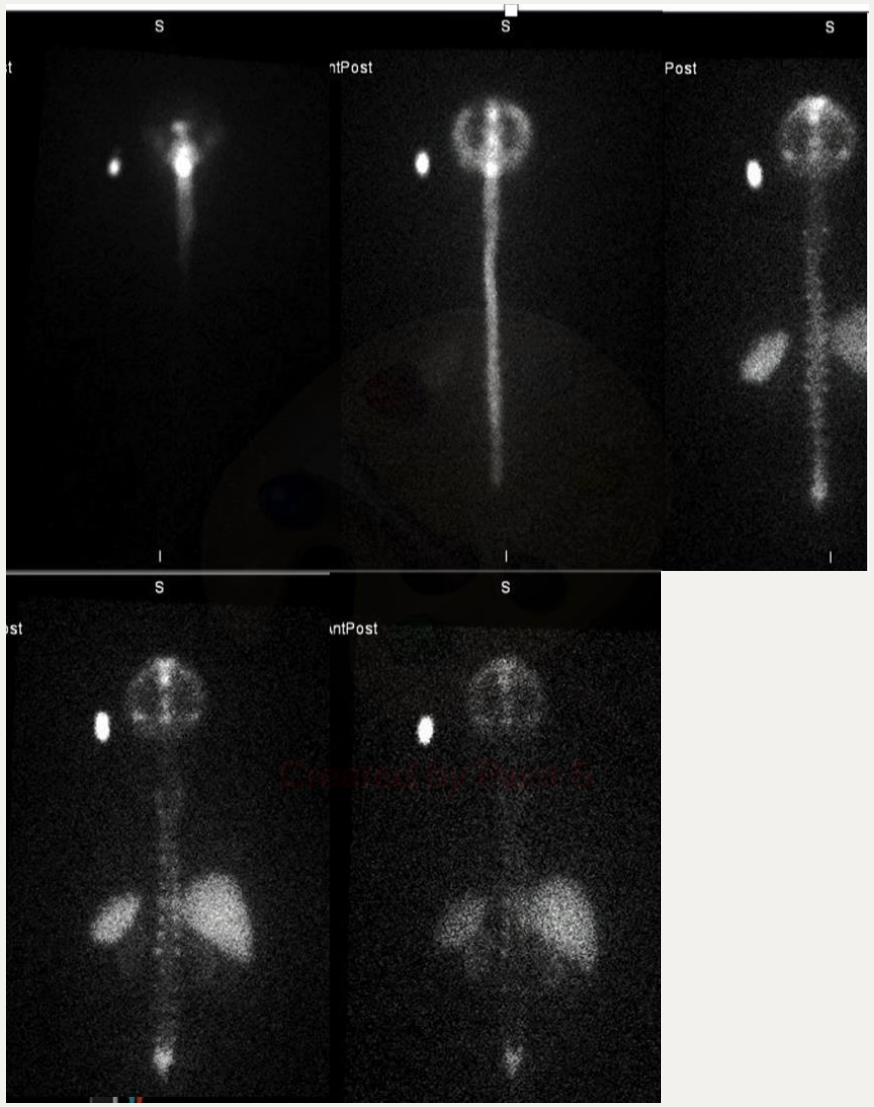
Region	Radiation Absorbed Dose (Gy)
Ventricles and cranial subarachnoid space	18.68
Ventricles (lateral, 3rd, and 4th)	6.83
Cranial subarachnoid space	25.32
Spinal Fluid	5.92



ReSPECT-LM Phase 1 Clinical Trial – Dose Escalation

Mays Cancer Center

Patient 01-101



Assessment: Tumor Cells/mL

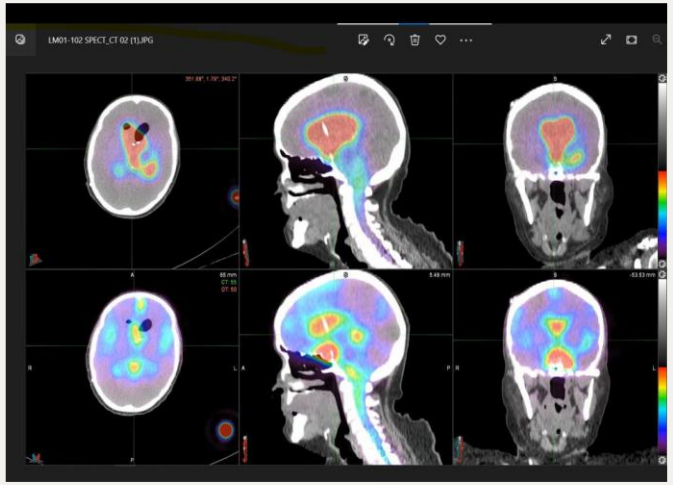
Pre	5 hrs	24 hrs	48 hrs	14 days	28 days	43 days	56 days
85.94	155	133.13	14.35	Not Req	40.16	Not Req	30.83

ReSPECT-LM Phase 1 Clinical Trial – Dose Escalation

Patient 01-102

- 60 year old white female
- Stage III Invasive **Lobular Breast Carcinoma** of the right breast (2016); bone metastases (06/2020), leptomeningeal metastasis (01/2022)
- Previous treatment with total mastectomy (10/2016) followed by chemotherapy and radiation in 2016-2017
- Enrolled in **Cohort 1** and treated with 6.6 mCi ^{186}RNL in 5.0 ml infusate on 15 June 2022

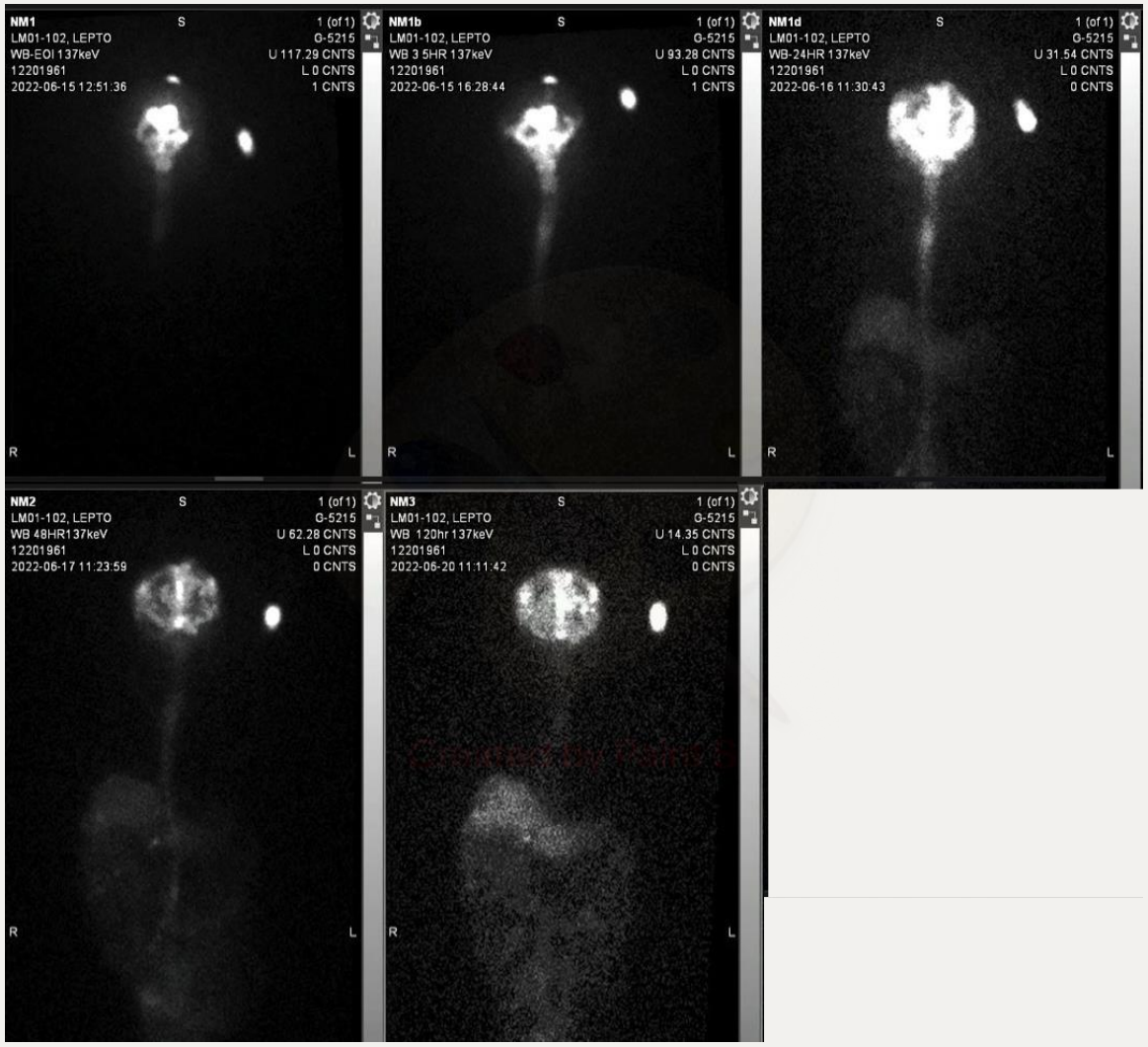
Region	Radiation Absorbed Dose (Gy)
Ventricles and cranial subarachnoid space	26.80
Ventricles (lateral, 3rd, and 4th)	36.44
Cranial subarachnoid space	21.25
Spinal Fluid	5.76



ReSPECT-LM Phase 1 Clinical Trial – Dose Escalation

Mays Cancer Center

Patient 01-102



Assessment: Tumor Cells/mL

Pre	5 hrs	24 hrs	48 hrs	14 days	28 days	43 days	56 days
839.13	551.03	455.29	506.73	Not Req	395.51	Not Req	1,133.40

ReSPECT-LM Phase 1, Part A Trial Complete

Summary

- 10 patients received single administration over 3 dosing cohorts
  - Radiation persists beyond 7 days in CSF
  - 50-90% reduction of tumor cells in CSF at 28 days following single administration (n=4)
  - Favorable safety profile, no DLTs
  - 8 out of 10 patient alive up to 1 year

Safety

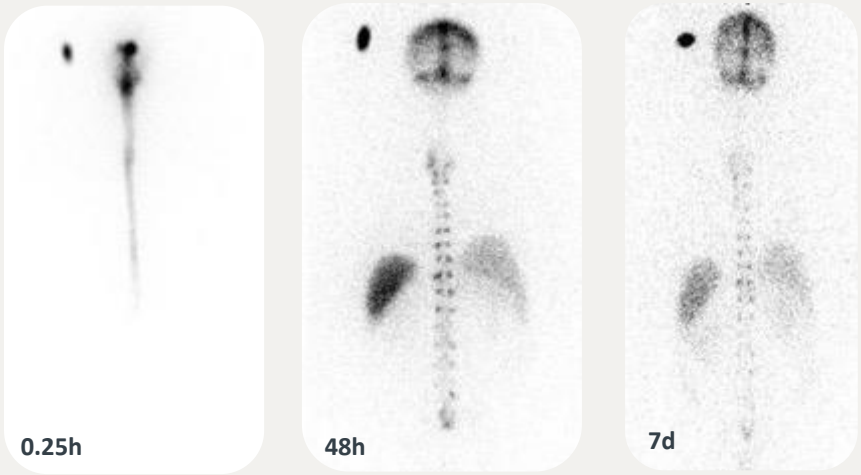
- No treatment emergent AEs greater than Grade 1
- Most common AE reported is headache
- Non-treatment-related AEs primarily related to SSKI administration

- 1 patient safely received second administration

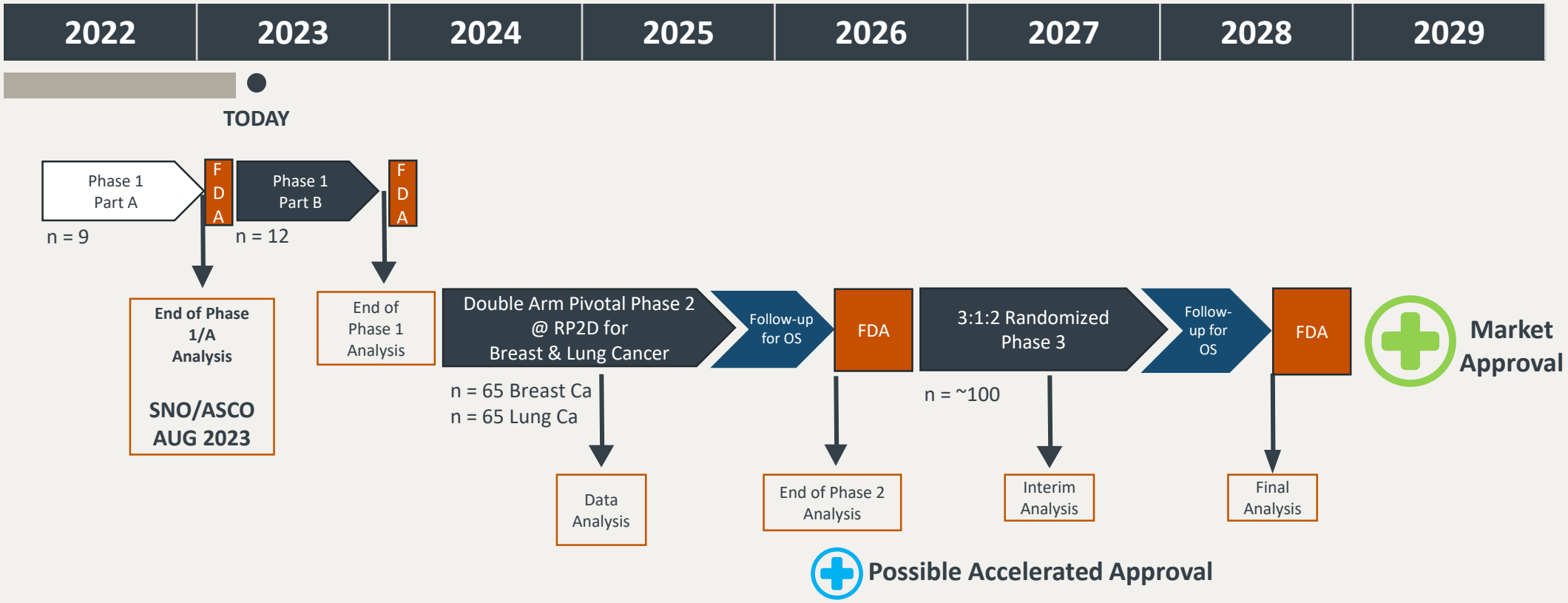
Phase 1, Part A Dose Escalation

Cohort	Infused Volume (mL)	Total ^{186}RNL Activity (mCi)	Concentration (mCi/mL)	Theoretical Maximum Absorbed Dose in CSF (Gy)	Ventricles & Cranial Subarachnoid Space
1	5.0	6.6	1.32	50	24.84
2	5.0	13.2	2.64	100	43.07
3	5.0	26.4	5.28	200	In analysis

Phase 1, Part A AP Planar SPECT



ReSPECT-LM Clinical Development Path for LM (Breast & Lung CA)



Notes:

- **Interim Analysis** – pooled analysis of Phase 1 + 2 + 3 dose data to assess delivery, dose, safety & efficacy to request potential accelerated approval with post-marketing commitment
- **Anticipated Phase 3 design** for either Breast or Lung Cancer, includes 3:1:2 randomization (100 treated + 33 standard of care + 66 propensity matched historical clinical trial control arm)
- **Follow-on studies** – investigating multidose, retreatment, and primary cancers outside of breast and lung



Selective Internal Radiotherapy (SIRT) for Solid Tumors

PLUS™ THERAPEUTICS

SIRT (Selective Internal Radiotherapy): Disease & Market Assessment

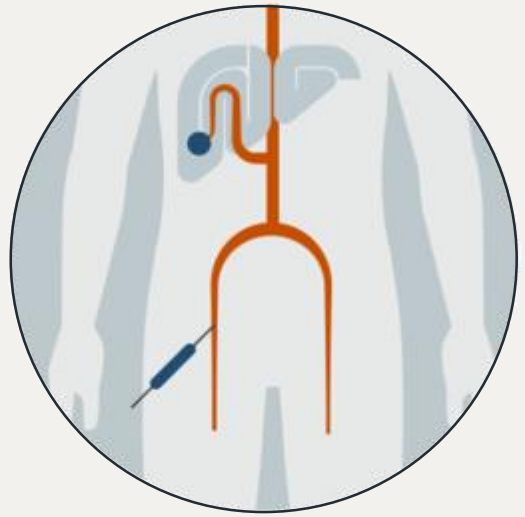
Currently an option for liver cancer- with potential to treat many solid tumors

Overview

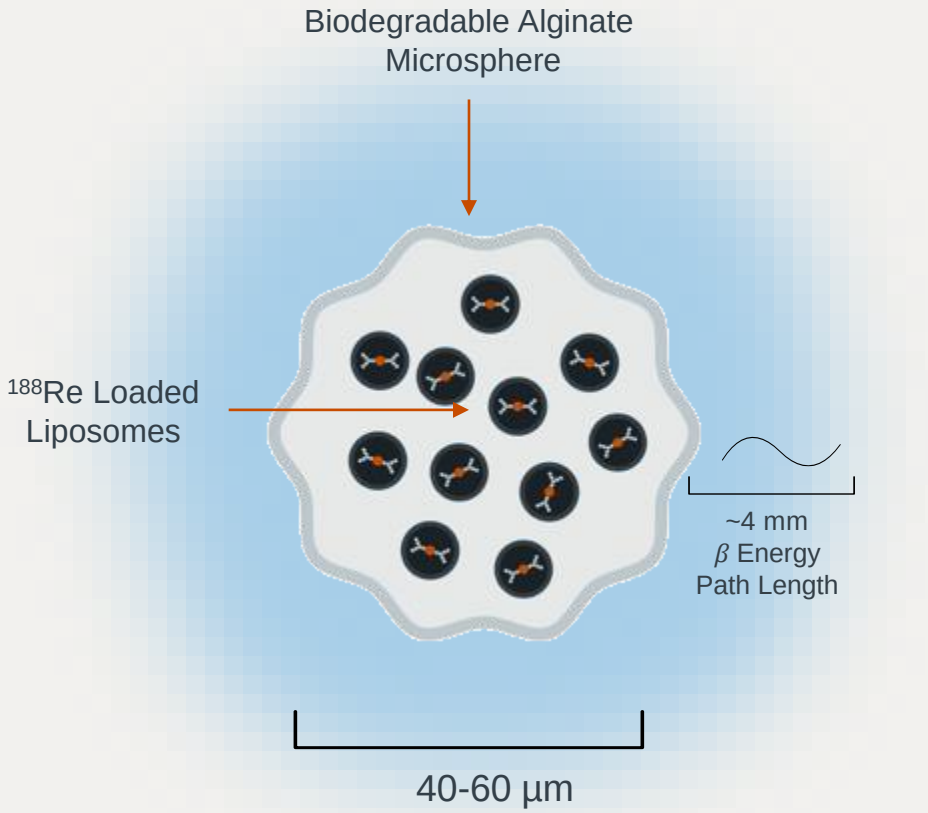
- SIRT is an angiographic procedure to administer radiotherapy treatment for cancer in the liver.
- Two Yttrium-90 glass/resin-based products used to treat >100K liver cancer patients over last 20+ years
- Increasingly common liver cancer treatment option despite lack of conclusive randomized clinical trial data
- Moderate growth expected in Asia-Pacific market due to highest liver cancer incidence

Opportunity

- Treat liver cancer (with expansion to cancers of the pancreas, prostate, head & neck, and GBM) with the first-ever ^{188}Re SIRT to extend life of patients using a safer, more targeted, & convenient treatment approach.
- Product Differentiation
  - Work-up (^{99m}Tc microsphere) predictive of final clinical outcome (^{188}Re microsphere)
  - Higher quality imaging (^{188}Re gamma photon)
  - Radioactivity retention (nanoliposome encapsulation)
  - Clearance (microsphere degradation)
  - Patient access, affordability, convenience



Re-188 Nanoliposome Biodegradable Alginate Microsphere (^{188}RNL-BAM)

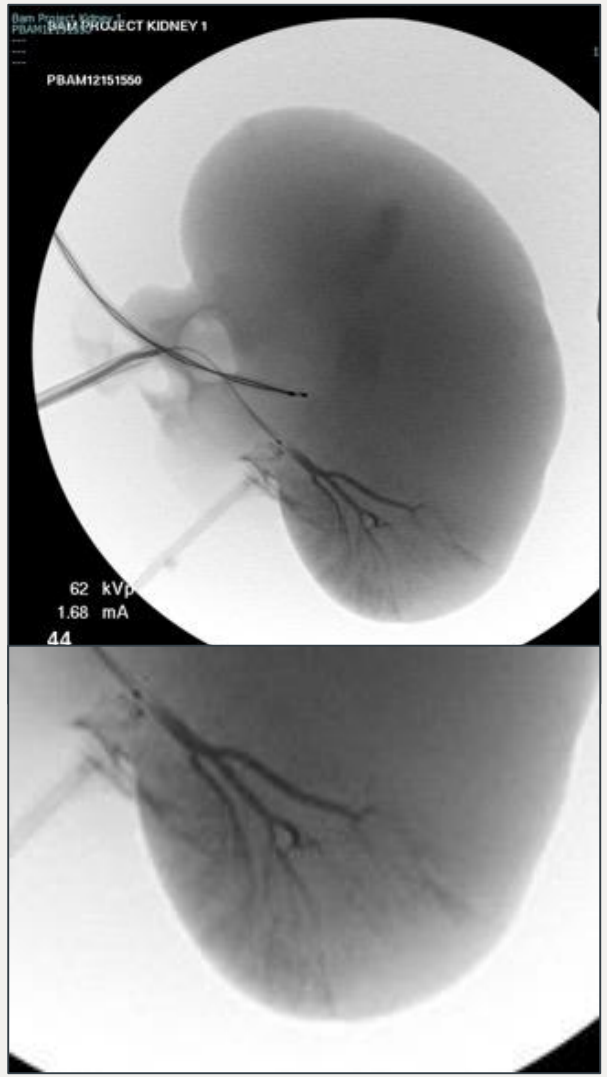


+ ^{188}Re loaded liposomes encapsulated in Alginate Microsphere
+ Only biodegradable SIRT therapy in development
+ ^{188}Re is a Dual energy emitter: beta (cytotoxic) & gamma (imaging)
+ Average path length ~4 mm
+ Patented encapsulation & loading process

^{188}RNL-BAM: Nonclinical *Ex-Vivo* Study

Proof-of-Concept Study

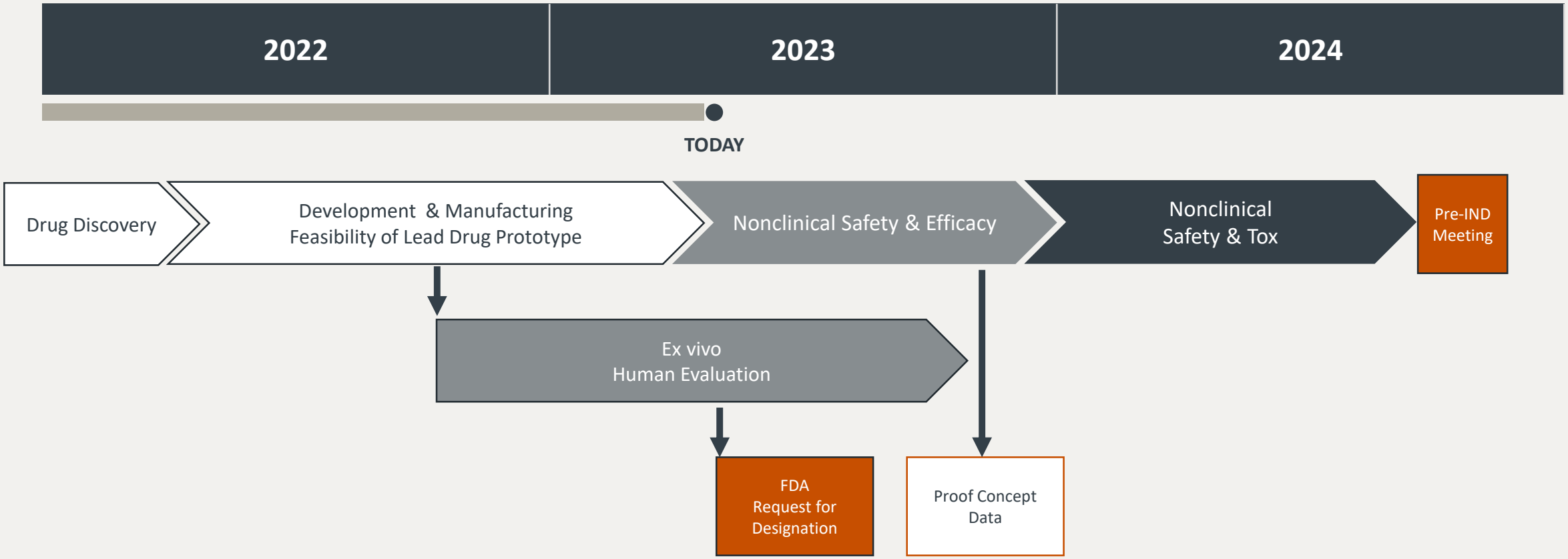
- Manufacturing feasibility complete
- Successfully tested ^{188}RNL-BAM in a proof-of-concept kidney perfusion model to evaluate drug and delivery parameters
- Confirmed effects of particle sizes on distribution of embolization
- Confirmed effects of ^{188}RNL-BAM microspheres on embolization volume



Human kidney ex vivo perfusion model

^{188}RNL-BAM

Clinical development path: Through Phase 1



2023 Milestones

Rhenium Re^{186} Obisbemeda | ReSPECT™ Clinical Trials

Recurrent Glioblastoma
+ Phase 1 dose escalation: peer-reviewed journal publication
+ Phase 1: Present Phase 1 data (Cohort 8) at SNO NOV 2023
+ Phase 2B: present interim data at SNO NOV 2023

Leptomeningeal metastases
+ Phase 1/Part A: present data at SNO/ASCO AUG 2023
+ Phase 1/Part B: initiate/complete enrollment

Pediatric Brain Cancer (ependymoma & high-grade glioma)
+ Phase 1: FDA IND approval
+ Phase 1: initiate enrollment

^{188}RNL-BAM

All Indications
+ Determine FDA regulatory designation
+ Present proof of concept preclinical data

Pipeline Expansion

+ Evaluate combination therapies in relevant preclinical models
+ Explore partnerships to expand CNS oncology opportunities
+ Submit multiple grant funding applications



Thank you

Marc Hedrick, MD
President & CEO

Andrew Sims
Chief Financial Officer

Norman LaFrance, MD
Chief Medical Officer

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