

PLUS THERAPEUTICS™

August 2021

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 and Section 21E of the Securities Exchange Act and are usually identified by the use of words such as “anticipates,” “believes,” “estimates,” “expects,” “intends,” “may,” “plans,” “projects,” “seeks,” “should,” “will,” and 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 and Section 21E of the Securities Exchange Act of 1934, as amended, and 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 and prospects, which are based on the information currently available to us and on assumptions we have made. Although we believe that our plans, intentions, expectations, strategies and 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 and will be affected by a variety of risks and factors that are beyond our control.

Risks and 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 and unexpected costs that may result therefrom; failure to realize any value of certain product candidates developed and being developed in light of inherent risks and difficulties involved in successfully bringing product candidates to market; inability to develop new product candidates and support existing products; the approval by the FDA and 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 and enforce patents and other intellectual property rights or the unexpected costs associated with such enforcement or litigation; inability to obtain and 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 and pricing pressures; economic recession and its negative impact on customers, vendors or suppliers; uncertainties of cash flows, expenses and inability to meet working capital needs; and other risks and uncertainties detailed in the risk factors section of Plus’ Form 10-K and 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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We believe in the critical importance in developing and delivering innovative, targeted radiotherapeutics for patients battling rare and CNS cancers.



PLUS

CNS & Rare Cancers

Responsible for Substantial Morbidity and Mortality Worldwide

- Significant unmet medical needs
  - 5-year survival of 36%
  - Few approved treatments
- Rare diseases
  - FDA ODD eligible
  - Sizeable aggregate population
- Biological overlap

FACTS ABOUT BRAIN TUMORS

An estimated **700,000+ PEOPLE** in the U.S. are living with a primary brain or central nervous system (CNS) tumor diagnosis:

210,000 WITH MALIGNANT TUMORS

490,000 WITH NON-MALIGNANT TUMORS

APPROXIMATELY

6-28%

OF ALL OTHER CANCERS LATER DEVELOP A CNS METASTASES



This accounts for **70,000 to 170,000** new patients diagnosed with CNS metastases each year.

IN 2020, NEW PRIMARY BRAIN TUMOR DIAGNOSES INCLUDED



70%

NON-MALIGNANT TUMORS
(58,860 Cases)

30%

MALIGNANT TUMORS
(24,970 CASES)

PRIMARY BRAIN TUMOR TYPES



- Meningioma (38%)
- Pituitary (17%)
- Glioblastoma (15%)
- Other Non-Glioma (11%)
- Other Glioma (11%)
- Nerve Sheath (9%)

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Sources: CBTRUS Statistical Report, NBTS

Glioblastoma

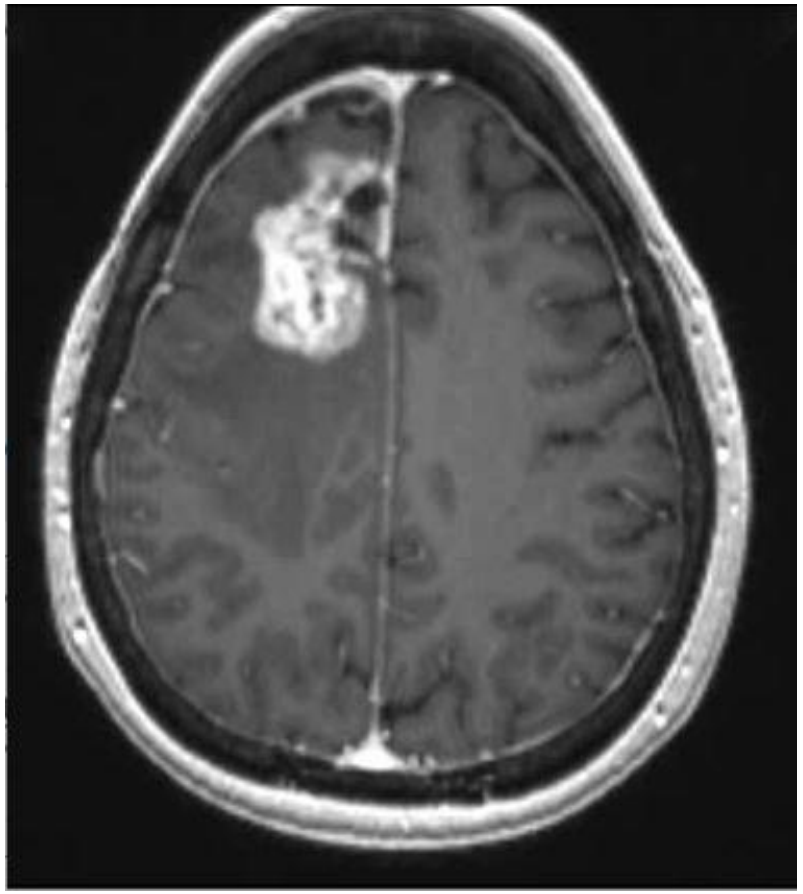
A Rare, Incurable, and Fatal Brain Cancer with No Good Treatment Options



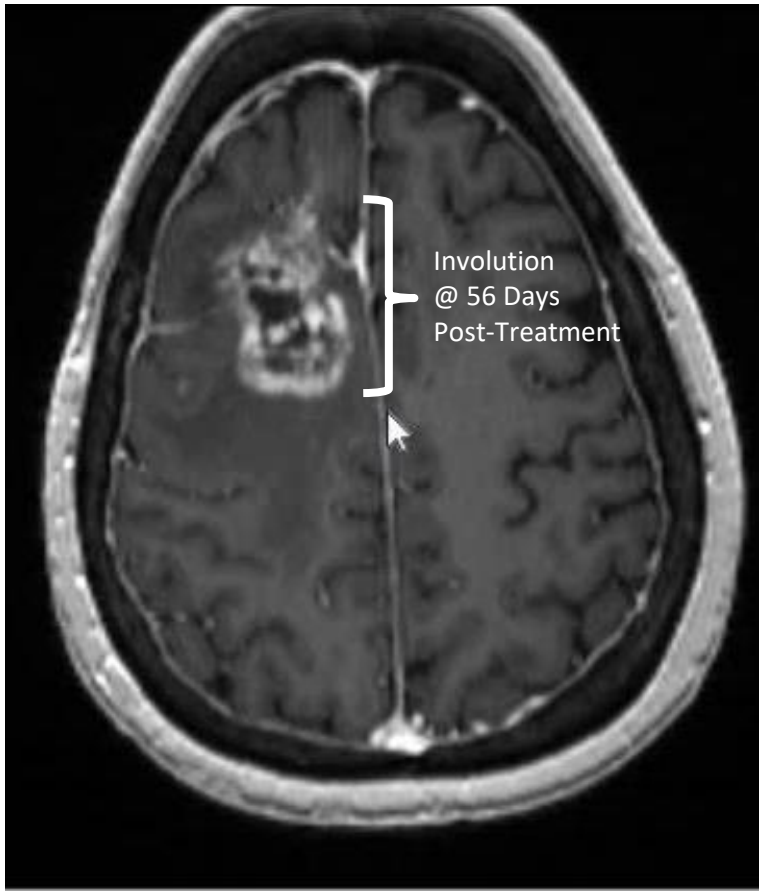
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PLUS Therapeutics: ReSPECT Dose Escalation Trial

Patient with Recurrent Glioblastoma- Before and After Tumor Ablation Following High Dose RNL Therapy



Before Treatment

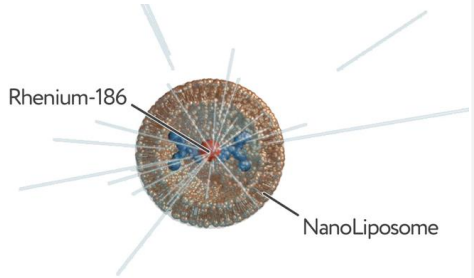


56 Days Post-Treatment

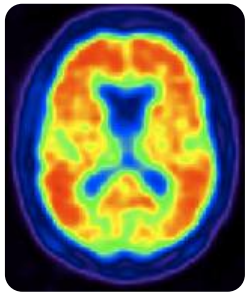
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PLUS Therapeutics: A Novel Approach to Intracranial Neoplasms

Marriage of New Developments Across Multiple Specialties



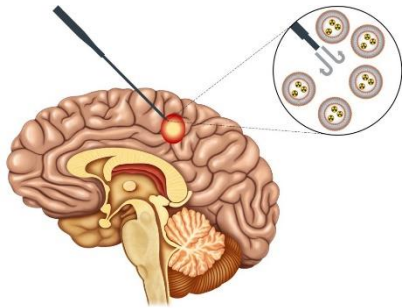
Nano Drug Delivery



Nuclear Medicine



Radiation Oncology

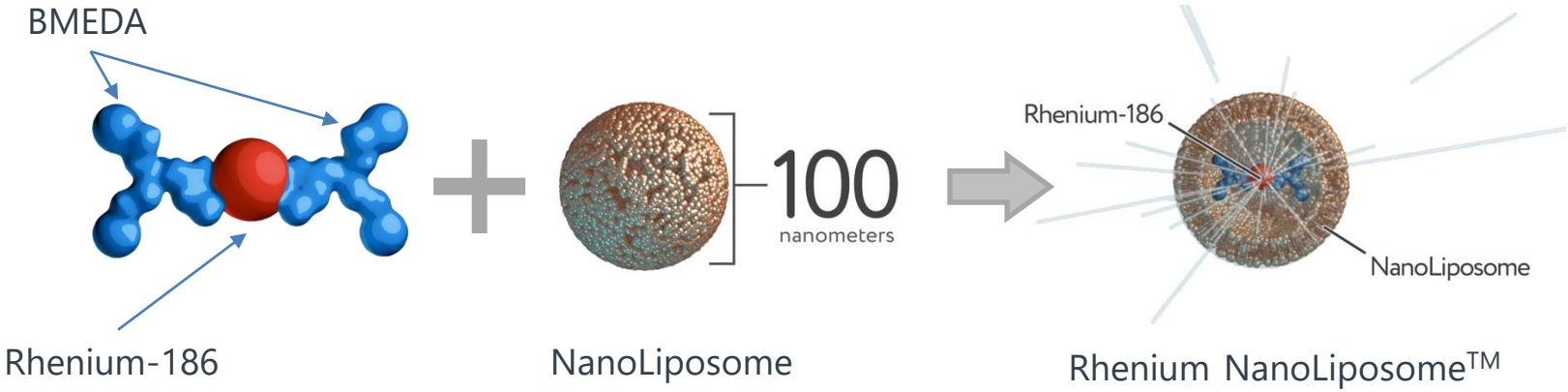


Neurosurgery

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Lead Asset: Rhenium Nanoliposome or RNL™

Proprietary Nanoscale Compound with a Unique Isotope



RHENIUM 186

- Dual energy emitter- Beta (cytotoxic) & Gamma (imaging)
- Short average path length- precision
- Low dose rate- safer for normal tissues
- High radiation density- overwhelms innate DNA repair mechanisms

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PLUS Therapeutics: Pipeline

Growing Preclinical and Clinical Therapeutic Pipeline

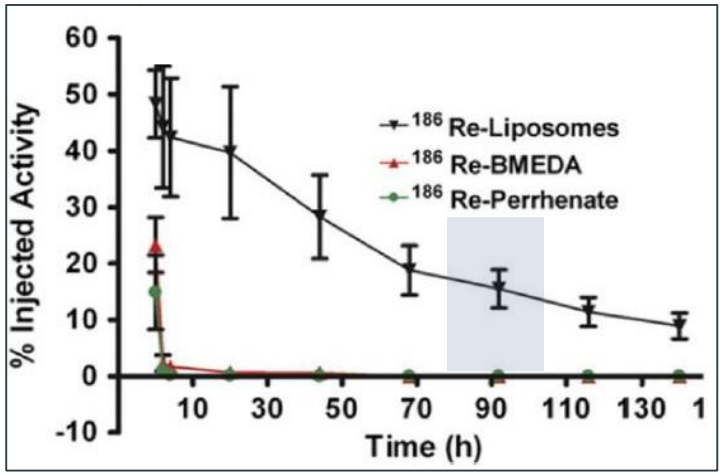
	Investigational Drug	Indication	Designation	Stage	External Funding
Monotherapy: Radiotherapeutic	**Rhenium NanoLiposome (RNL™)**	Recurrent Glioblastoma	FDA Orphan Drug FDA Fast Track	Phase 1	NIH/NCI to PII
		Leptomeningeal Cancer	-	IND pending	-
		Pediatric CNS Cancers: Ependymoma, High Grade Glioma & Diffuse Intrinsic Pontine Glioma	-	IND pending	-
Combination Therapy: Chemotherapeutic & Radiotherapeutic	**Doxorubicin & Rhenium NanoLiposome (DRNL™)**	Multiple	-	Preclinical	-

Plus DocePLUS™ and DoxoPLUS™ clinical-stage chemotherapeutic assets available for partnering

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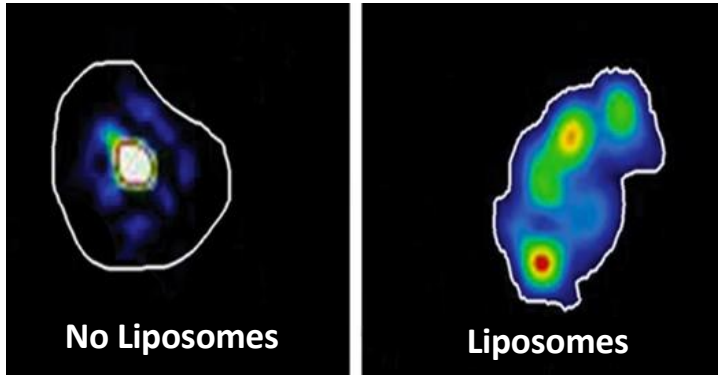
Spatiotemporal Behavior of RNL™ Following Brain Delivery

Prolonged Half-Life and Brain Retention



Tumor Retention

Liposomal encapsulation significantly extends the *in vivo* intracranial half-life of rhenium-186 (90 hours) and decreases clearance rate from the brain.



Tumor Dispersion

Liposomal encapsulation significantly extends rhenium-186 retention within the tumor and therefore improves dispersion characteristics in tissues.

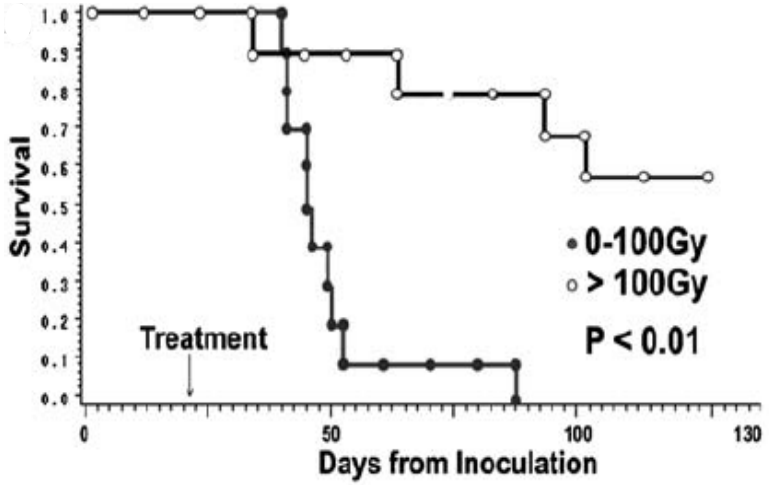
PLUS™ THERAPEUTICS

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

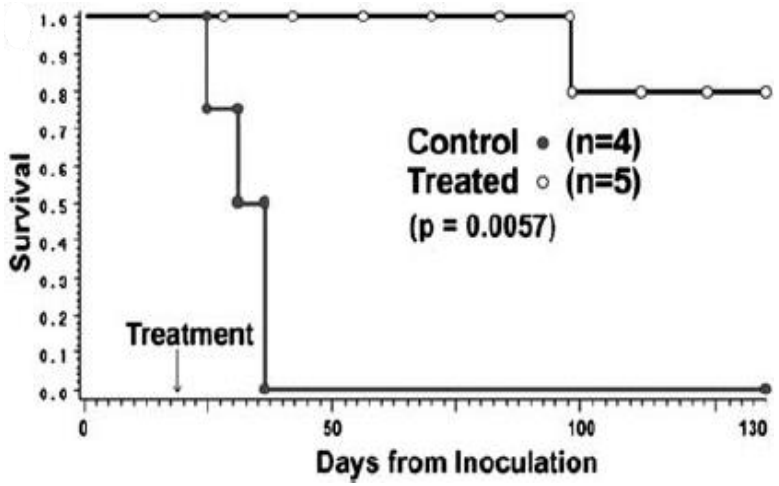
RNL™ Preclinical Data

RNL Significantly Prolongs Survival in U87 & U251 Intracranial Xenograft Models

U87



U251



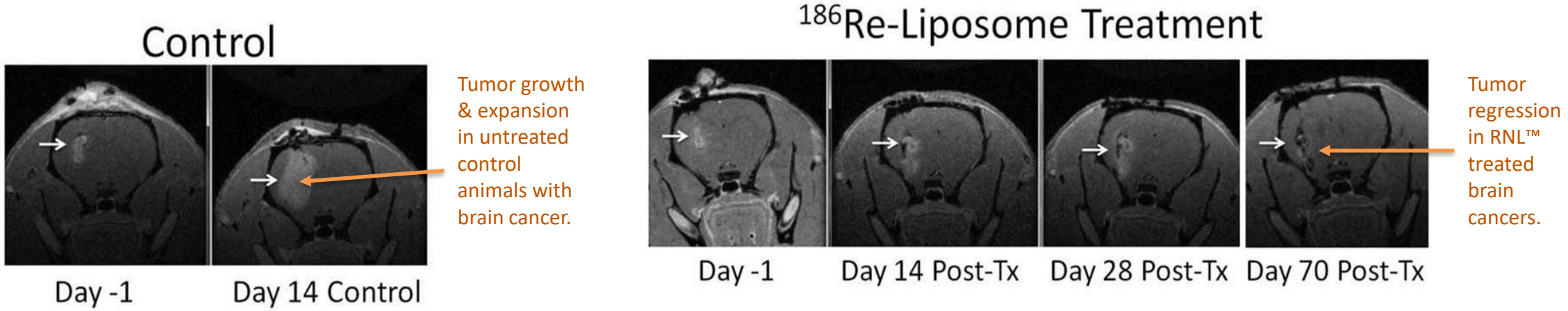
- Doses of up to 1,845 Gy were tolerated without weight loss or neurological deficit.
- No maximum tolerated dose of RNL reached.
- Statistically significant prolongation in survival, limited only be the end of the experiment.
- Blinded histologic analysis by neuropathologist showed no residual tumor all treated animals.

PLUS™ THERAPEUTICS

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

RNL™ Preclinical Data

Tumor Regression in U87 & U251 Intracranial Xenograft Models



- Bioluminescence assay showed many of the treated animals had a loss of activity to background levels suggesting complete eradication of the tumor.
- MRI analysis (above) supported the observation of tumor eradication.
- Blinded histologic evaluation by neuropathologist showed no residual disease.

PLUS™ THERAPEUTICS

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

RNL™ Fits Within Modern Clinical Workflows

Plan, Administer, and Confirm RNL™ Treatment with the Latest Imaging & Surgical Techniques



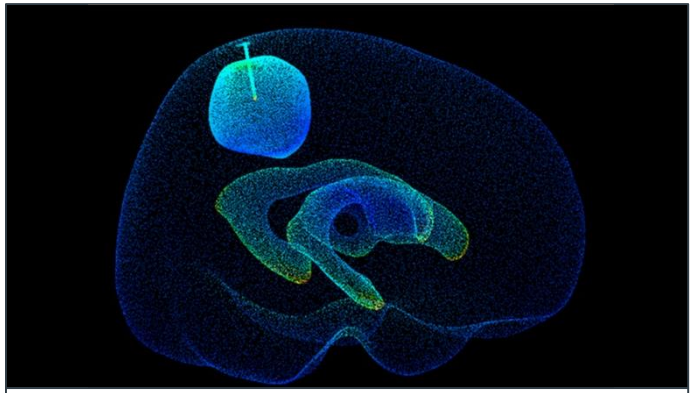
Preoperative targeting & surgical planning



Modern neurosurgical operating theater



Stereotactic catheter placement



Convection enhanced drug delivery

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Images courtesy of Brainlab; Convection enhanced delivery of chemotherapeutic drugs into brain tumour, WenboZhan[a]Chi-HwaWang[b], Imperial College London, UK and National University of Singapore, 20 December 2017.

RNL™ for Recurrent Glioblastoma

Potential Advantages Compared to External Beam Radiation Therapy



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RNL™ for Recurrent Glioblastoma

Phase 1/2 Clinical Trial Design

Multi-center, sequential cohort, open-label, volume and dose finding study of the safety, tolerability, and distribution of ^{186}RNL 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, followed by an expansion at the designated recommended phase 2 dose (RP2D).
+ Maximum number of planned subjects: up to 55 subjects (including patients enrolled in the Phase 1 dose escalation trial and a subsequent cohort at the RP2D).
+ Supported by a NIH/NCI grant through Phase 2.

ClinicalTrials.gov: NCT01906385

Enrollment Update

Cohort	Infused Volume (mL)	Total RNL™ Activity (mCi)	Concentration (mCi/mL)	Average Absorbed Dose (Gy)	Status
1	0.66	1.0	1.5	198	**Enrolling cohort 8** **(n = 22 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	
6	8.80	22.3	2.5	287	
7*	**8.80**	**22.3**	**2.5**	**584**	
8	**12.3**	**31.2**	**2.5**	**TBD**	

*Cohort 7 utilized same volume and dose as cohort 6 but with increase in maximum flow rate to 20 microliters/minute

Safety Update

RNL Is Safe and Well Tolerated

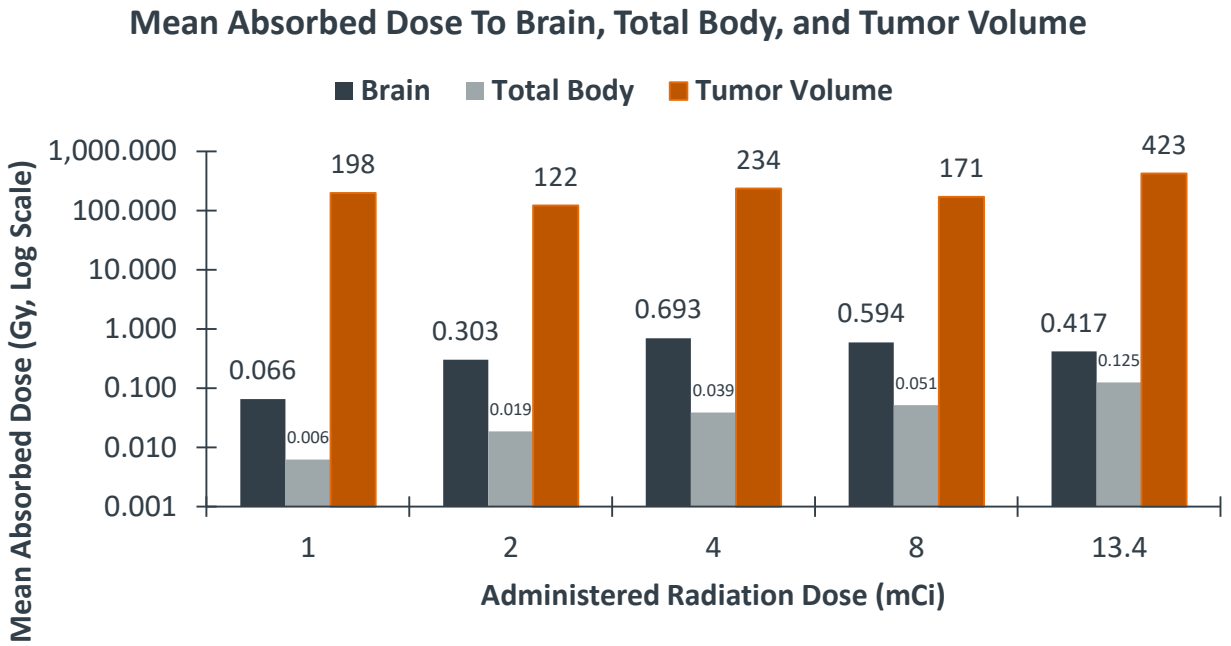
Thus far, in the Phase I study of 22 subjects in 8 dosing cohorts with recurrent Glioblastoma (GBM) receiving a single dose of RNL™:

- RNL™ appears to be safe and well-tolerated.
- There have been no dose limiting toxicities.
- The majority of AEs reported were mild or moderate (Grade 1 or 2) in intensity.
- Most AEs were considered causally unrelated to RNL™ except scalp discomfort, which was considered related to the surgical procedure.
- No meaningful differences or patterns in the incidence of related treatment emergent adverse effects reported across individual treatment groups or cohorts.
- Neither the incidence nor severity of AEs appeared to increase with increasing doses of RNL™.

Dosimetry Evaluation

High Absorbed Doses to Tumor Volume, Not Brain or Total Body

- Maximum tumor absorbed dose 740 Gy
- Absorbed Dose (Gy) to Tumor Volume
  - Median absorbed dose- 334 Gy (range 9-740 Gy)
- Ratio of mean tumor volume AD/mean total body AD in cohorts 4 & 5, ≥ 3,000



Radiation Delivery Update

Cohort 5 – 8 study higher drug volumes and radiation dosages

- No delivery failures
- Safely deliver up to 740 Gray of radiation to tumors
- Mean absorbed radiation dose to the tumor- 392 Gy.
- 1 to 4 catheters used for delivery
- Mean percent tumor covered- 90%
- Poor convection with prior Bevucizamab therapy- enrollment excluded

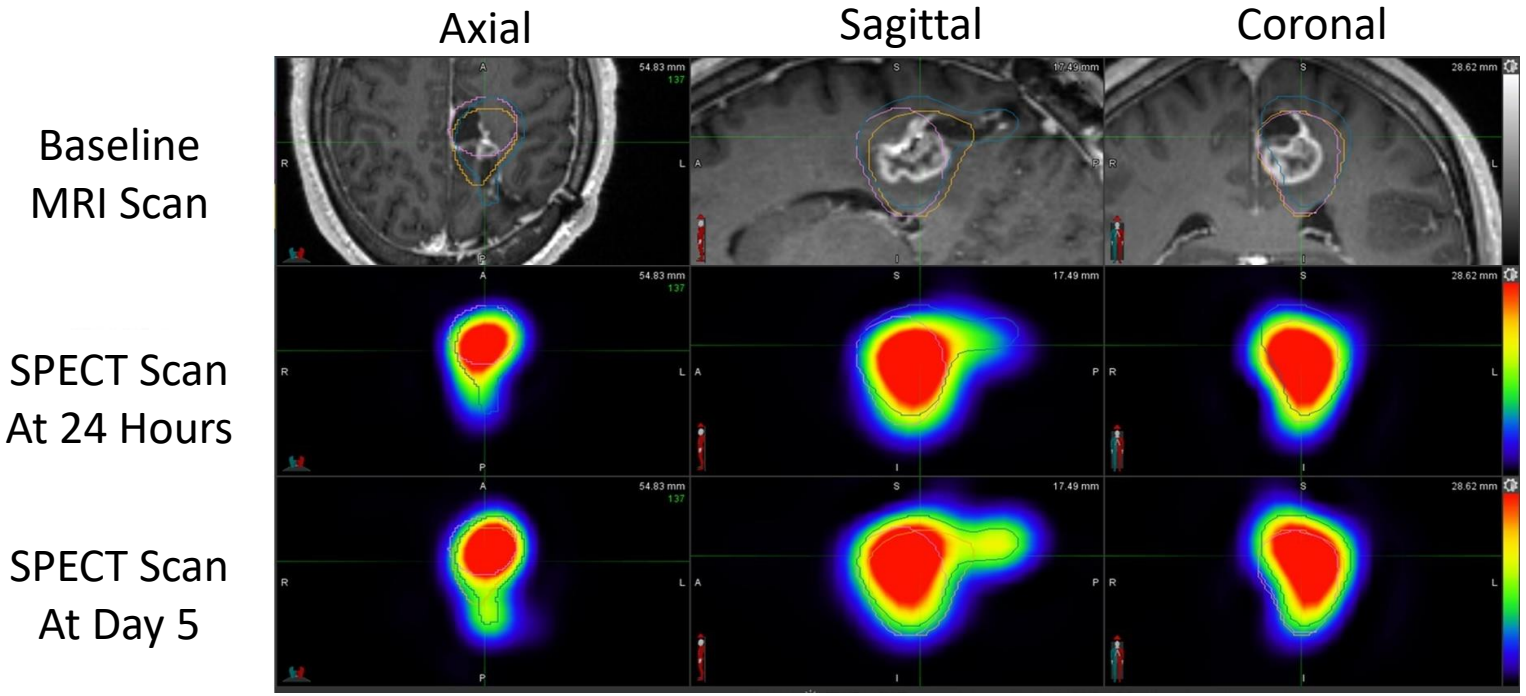
Treatment Effect on Overall Survival

Potential survival benefit of RNL with adequate drug delivery

- ReSPECT update as of August 1, 2021:
  - 8 of 22 treated remain patients alive
  - 13 patients enrolled between 2015 to 2019:
    - 5/13 had absorbed tumor radiation doses > 100 Gy & tumor coverage percentage > 75%
    - The average overall survival in these 5 patients is 769 days
    - 2 patients still alive
  - 9 patients enrolled since 2020:
    - 7/9 had absorbed tumor radiation doses > 100 Gy & tumor coverage percentage > 75%
    - The average overall survival in these 7 patients is 173 days
    - 6 patients are still alive

Tumor Coverage and Retention

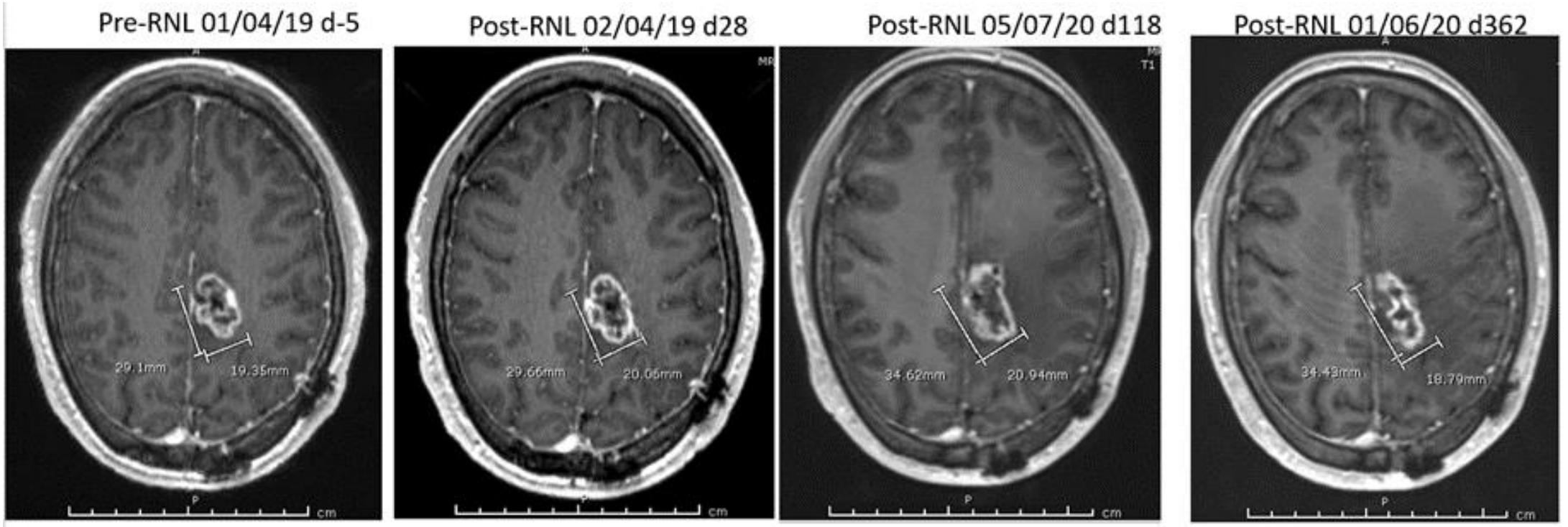
Subject 01-014



- Tumor volume was 6.5 mL and tumor coverage was > 90%
- Absorbed dose delivered to tumor was 419 Gy

Natural History of Recurrent GBM Lesions After RNL™

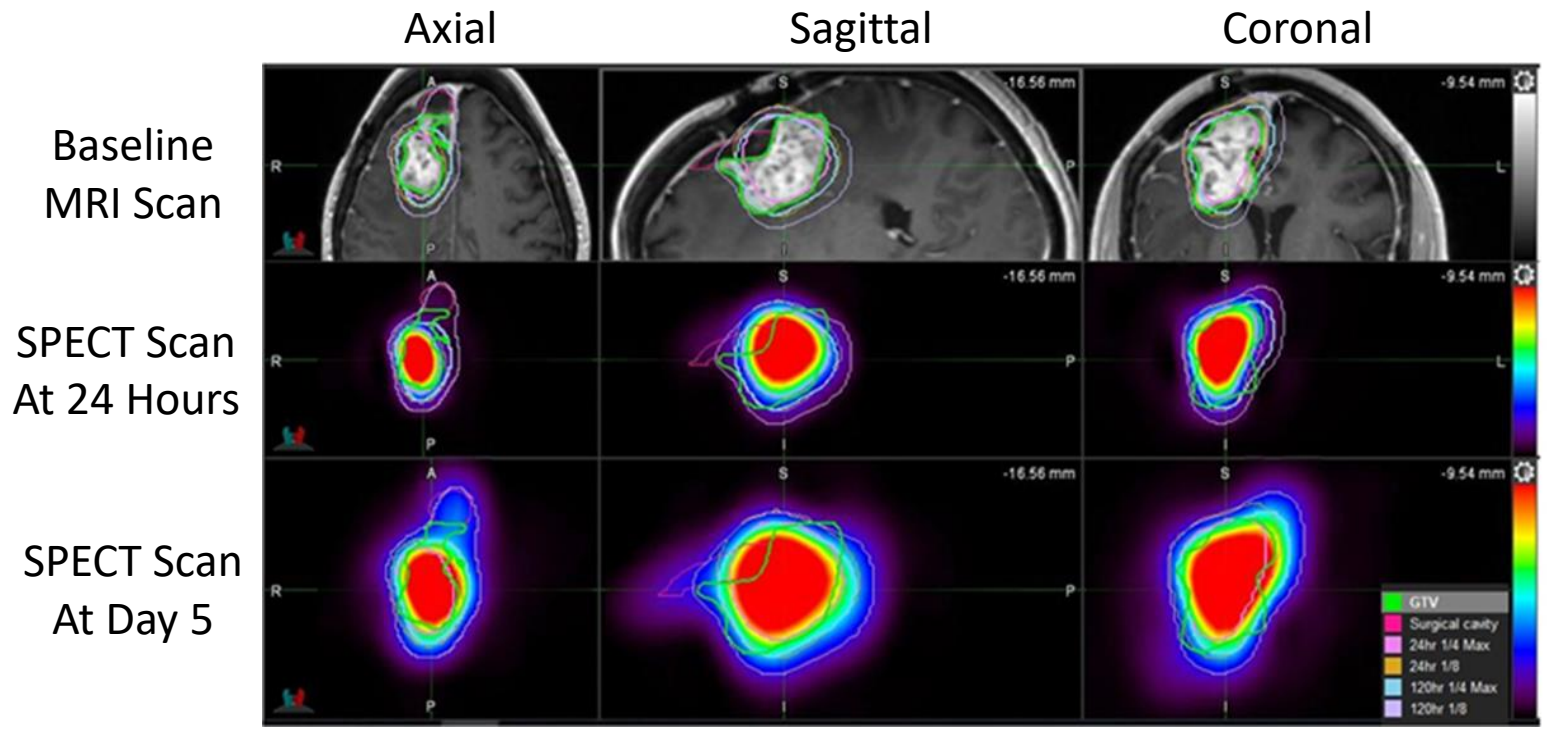
Subject 01-014: Tumor Response Observed to Day 362



- MRI scans revealed an initial increase in size which peaked at Day 118, with some associated edema, followed by tumor shrinkage out to at least Day 362
- Patient remains alive (>900 days)

Tumor Coverage and Retention

Subject 01-017

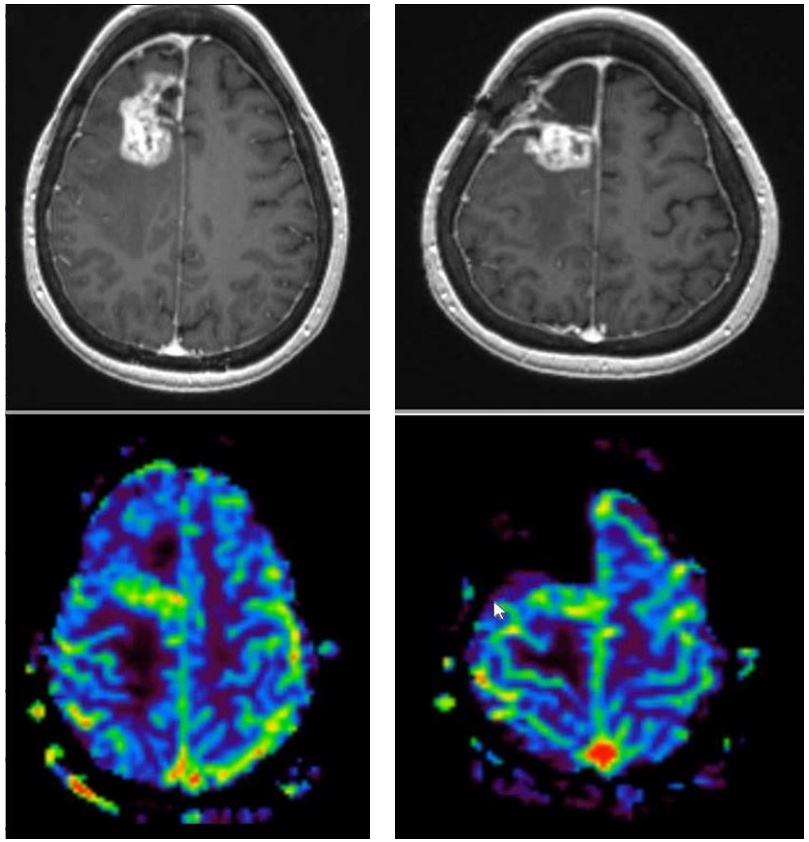


- Tumor volume was 18.8 mL and tumor coverage was 87%
- Absorbed dose delivered to tumor was 336 Gy

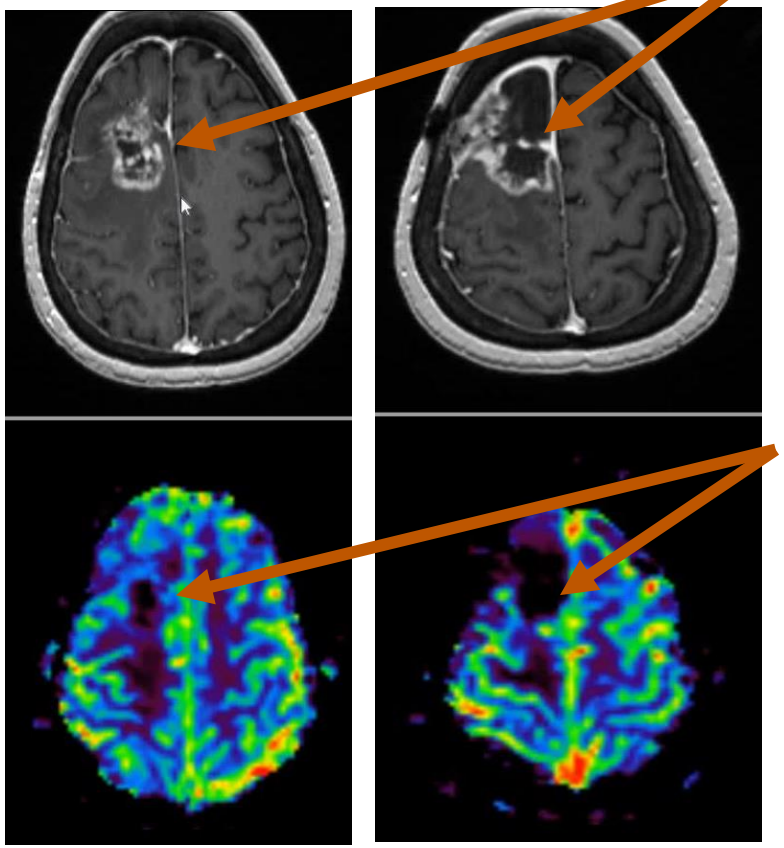
MRI & Perfusion Imaging

Subject 01-017: Tumor Ablation & Loss of Perfusion

Pre-Treatment



Day 56



RNL™ Indication Expansion

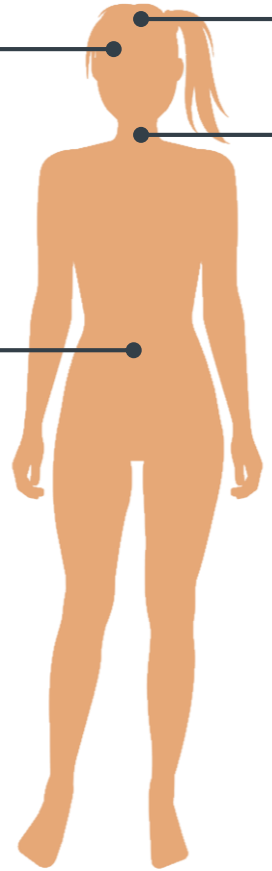
Opportunity to Address Significant Unmet Needs for Multiple Rare Cancers

Leptomeningeal Carcinomatosis (LMC)

+ U.S. annual incidence: 110,000
+ Derived from breast/lung cancers, melanoma, GI malignancies
+ No clear SoC: radiation & chemo used
+ 5-year survival: unreported
+ Survival if untreated: 4-6 weeks
+ Survival if treated: 4-6 months

Peritoneal Carcinomatosis

+ U.S. annual incidence: 72,000
+ Derived from colorectal/gastric/ovarian/pancreatic cancers
+ Controversial SoC: chemo & cytoreduction surgery
+ 5=year survival <3%-66%



Pediatric Brain Cancer

+ U.S. annual incidence: 1,000*
+ Current SOC: steroids, radiation, surgery &/or chemo
+ 5-year survival: <3% (DIPG), <20% (HGG), 75% (Ependymoma)
+ Median survival: 10-11 months (DIPG)

Head & Neck Squamous Cell Carcinoma

+ U.S. annual incidence: 53,000
+ Current SoC (locally advanced tumors): radiation, surgery, systemic therapy
+ Current SoC (small tumors without nodal involvement): radiation or surgery
+ 5-year survival: 66%
+ 30-40% develop recurrent locoregional cancer
+ 20-30% develop metastatic disease
+ Median OS in recurrent or metastatic: 6-15 months

* High Grade Glioma, Ependymoma, Diffuse Intrinsic Pontine Glioma

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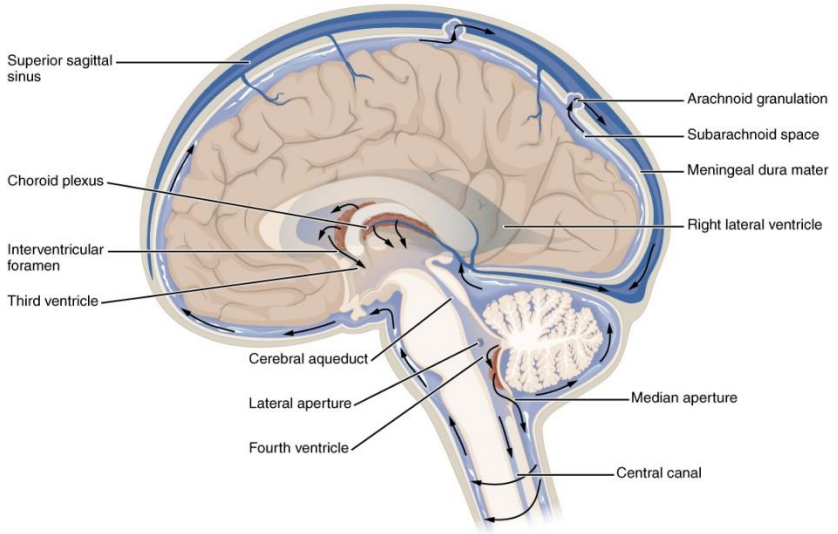
RNL™ Rationale for Leptomeningeal Cancer

Disease Background

+ Leptomeningeal cancer, also known as carcinomatosis, is a cancer that starts in one part of the body spreads to the leptomeningeal lining of the brain and spinal cord surrounding the CSF space.

100 nm NanoLiposomes in CSF

+ Circulate feely throughout the CSF.
+ Migrate to meningeal surfaces where LMC is located.
+ Have an extended half life - several weeks vs. hours with unencapsulated drugs.



Preclinical Data

+ Unpublished data suggests RNL may be effective in preclinical models of leptomeningeal cancer

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Pre IND Meeting Feedback on Potential New RNL Indications

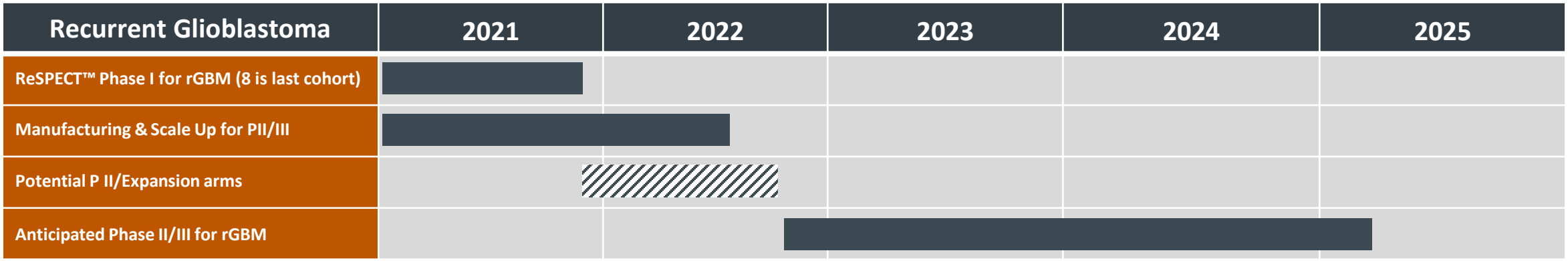
Leptomeningeal Disease

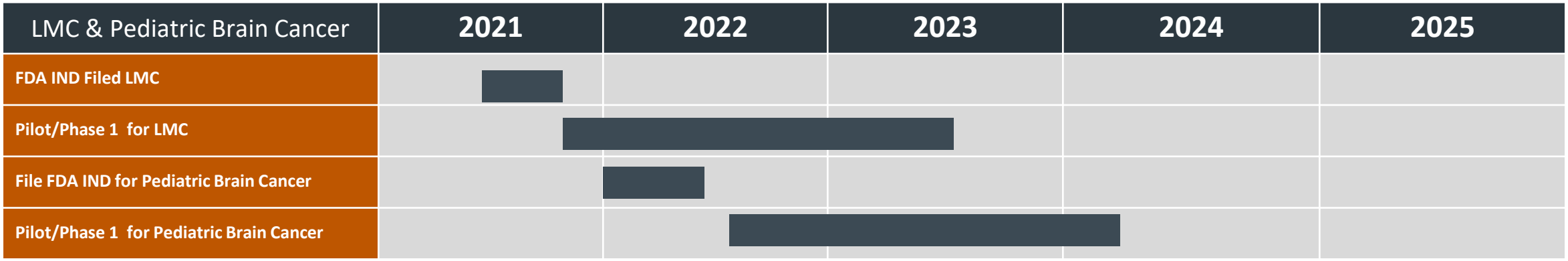
- Additional GLP toxicology studies are not needed to support initiation of the pediatric study.
- They provided constructive feedback on the study synopsis that should be helpful as a full protocol is developed.
- They provide helpful guidance on the data required for dose justification and suggest that we request a formal meeting to review division recommended phase 2 dose (RP2D) and prior to evaluation of expansion cohorts or trials designed to demonstrate efficacy and safety

Pediatric Brain Cancer Disease

- Additional GLP toxicology studies are not needed to support initiation of the pediatric study.
- They provided constructive feedback on the study synopsis that should be helpful as a full protocol is developed.
- They are requesting the study design be modified to include separate dose escalation components for each proposed anatomic tumor location.

RNL™ Development Plan





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Forthcoming Milestones for 2021 and into 2022

- Complete enrollment & report data from U.S. ReSPECT™ Phase I trial for RNL™ in recurrent GBM in 2021
- Complete CMC activities for RNL™ for a phase III drug supply
- Based on cohort 8 data, consider expansion cohort & finalize phase II/III plans
- Move RNL™ into Phase I for leptomeningeal and pediatric brain cancer
- Complete additional preclinical studies for RNL™ and DRNL™
- Potential acquisition, in-license new drug development candidates
- Partner RNL™, DocePLUS™ & DoxoPLUS™ assets if possible

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Capitalization Summary

Select Data (as of June 30, 2021)	
Cash	$17.2M
Common Shares Outstanding	12,087,525
Series U warrants	2,141,000
Senior Term Loan Principal (matures 2024)	$4.3M

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+ **Headquarters:** Austin, Texas, USA
+ **Manufacturing:** San Antonio, Texas, USA
+ **Nasdaq:** PSTV
+ **Corporate Website:** PlusTherapeutics.com
+ **ReSPECT™ Website:** ReSPECT-Trials.com