

PLUS™ THERAPEUTICS

Corporate Presentation

February 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 and urgency in developing and delivering complex, innovative treatments for patients battling rare CNS cancers.



PLUS

PLUS Therapeutics: Snapshot

Committed to Developing Novel, Targeted Therapies for Rare and Difficult to Treat CNS Cancers



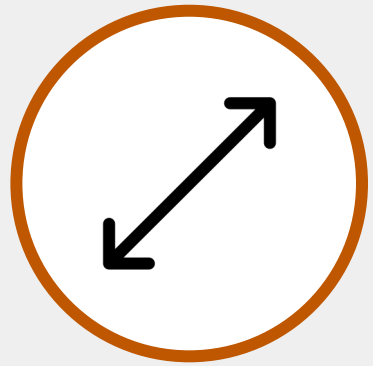
Proprietary and versatile nanoscale radiotherapeutic platform.



Focus on improving patient survival and quality of life.



Lead investigational drug is being evaluated in a NIH-funded clinical trial for recurrent brain cancer.



Preclinical data supports advancing new drug candidates into the clinic for other rare CNS cancers with significant unmet needs.

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CNS Cancers

Responsible for Substantial Morbidity and Mortality Worldwide

- Significant unmet medical needs
  - 5-year survival – 36%
  - Few approved treatments
- Rare diseases
  - FDA ODD eligible
  - Sizeable aggregate population
- Pathophysiologic 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%)

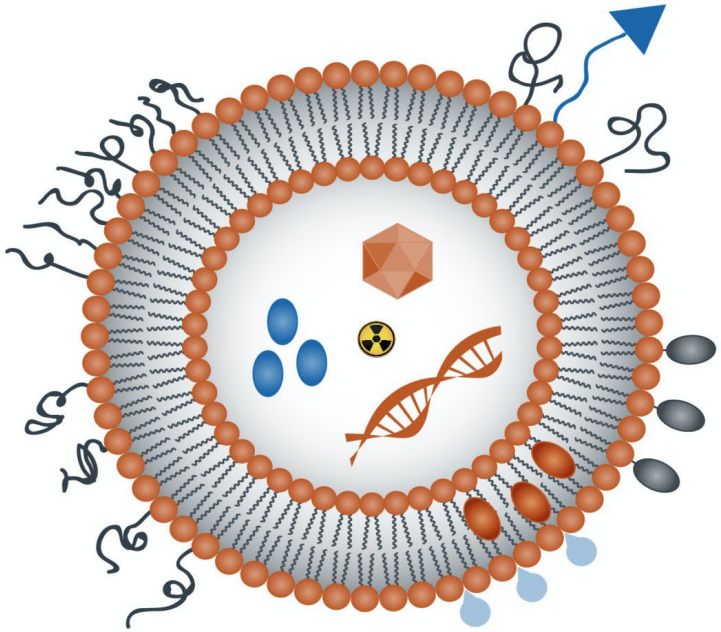
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Sources: CBTRUS Statistical Report, NBTS

PLUS Therapeutics: Platform

Nanoscale Drug Development Capability and Technology

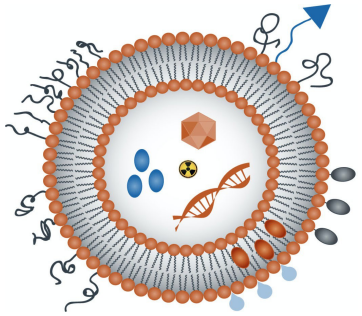
+ Drug encapsulation
+ Diverse compound loading (radionuclides, small molecules)
+ Protein membrane stabilization technology
+ Development facility in Texas
+ Manufacturing & scale up
+ Multiple FDA IND approvals & completed clinical trials



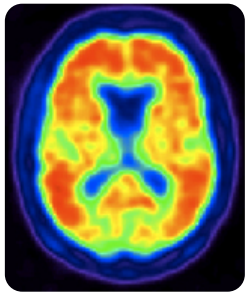
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PLUS Therapeutics: A Novel Approach to Intracranial Neoplasms

Marriage of New Developments in Multiple Arenas



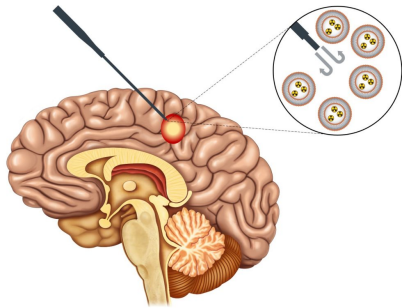
Nano Drug Delivery



Nuclear Medicine



Radiation Oncology

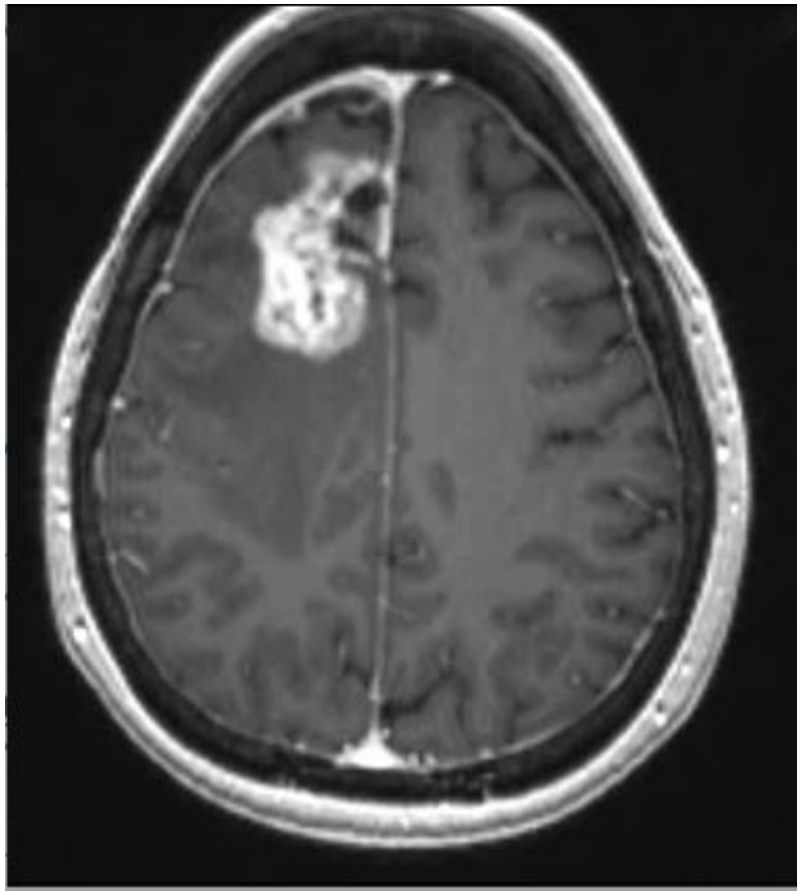


Neurosurgery

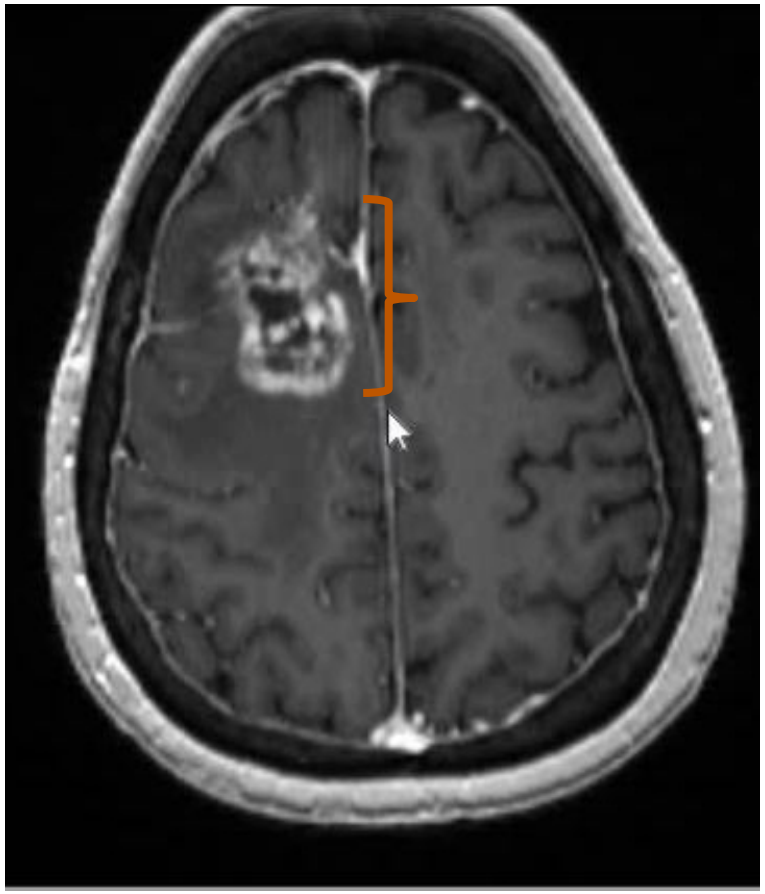
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PLUS Therapeutics: Encouraging Phase I Data

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: Pipeline

Progress with Rhenium-Based Therapies Across Both Preclinical and Clinical Programs

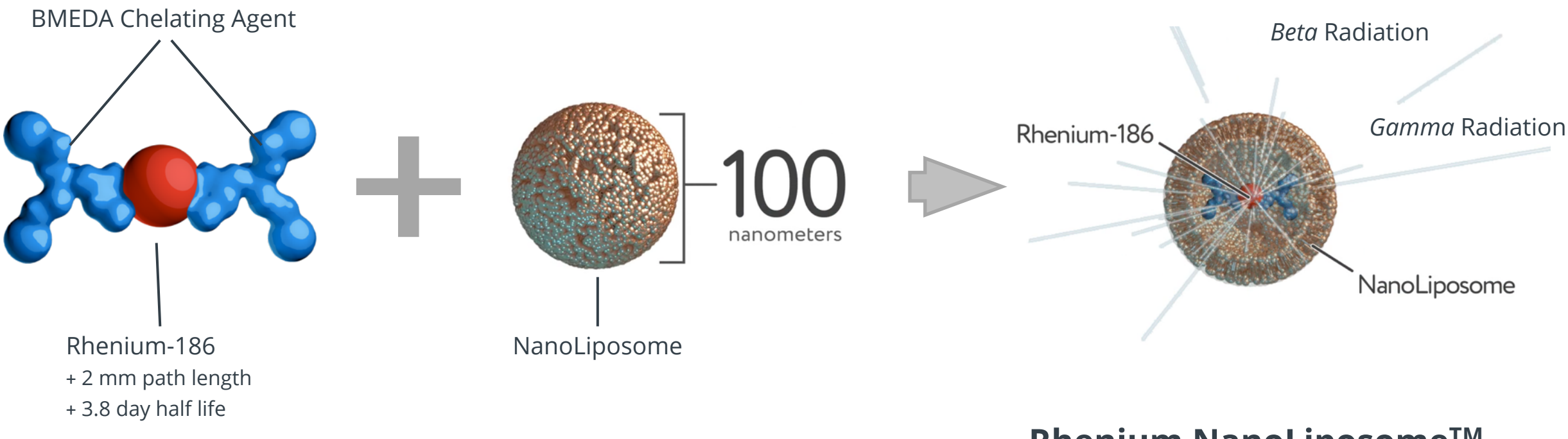
Modality		Investigational Drug	Indication	Designation	Stage	External Funding
	**Monotherapy: Radiotherapeutic**	**Rhenium NanoLiposome (RNL™)**	Recurrent Glioblastoma	FDA Orphan Drug FDA Fast Track	Phase 1	NIH/NCI
			Leptomeningeal Cancer	-	Pre-IND	-
			Pediatric CNS Cancers	-	Pre-IND	-
	**Combination Therapy: Chemotherapeutic & Radiotherapeutic**	**Doxorubicin & Rhenium NanoLiposome (DRNL™)**	Multiple	-	Preclinical	-

Plus 2 additional clinical-stage chemotherapeutic assets available for partnering

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Lead Asset: Rhenium Nanoliposome or RNL™

Proprietary Nanoscale Therapy Emitting Two Types of Radiation



Rhenium NanoLiposome™

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Glioblastoma

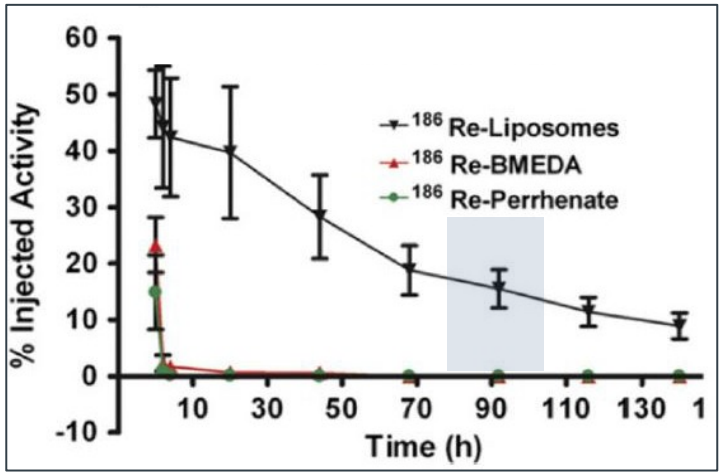
A Rare, Incurable, and Fatal Brain Cancer with No Good Treatment Options



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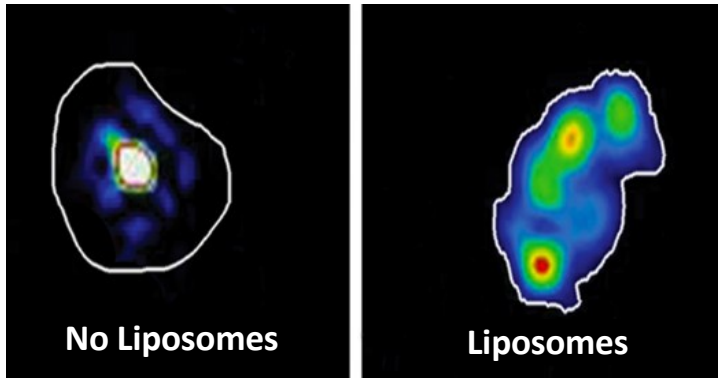
RNL™ Preclinical Data

Prolonged Tumor 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

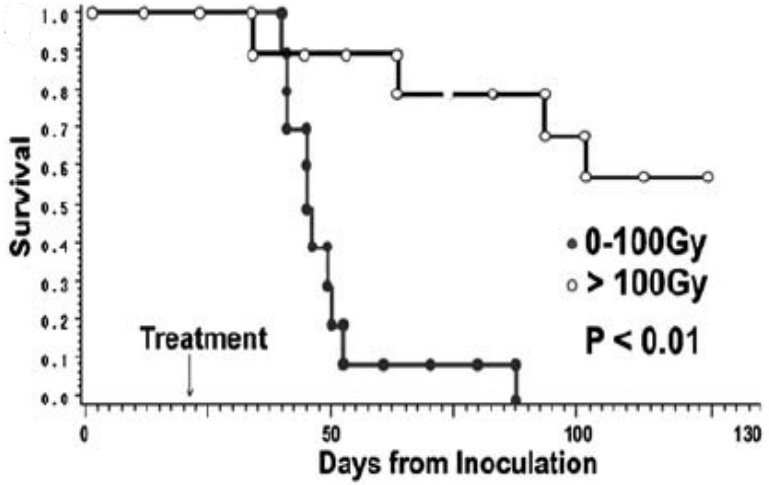
Liposomal encapsulation significantly extends rhenium-186 retention within the tumor and therefore improves dispersion characteristics in tissues.

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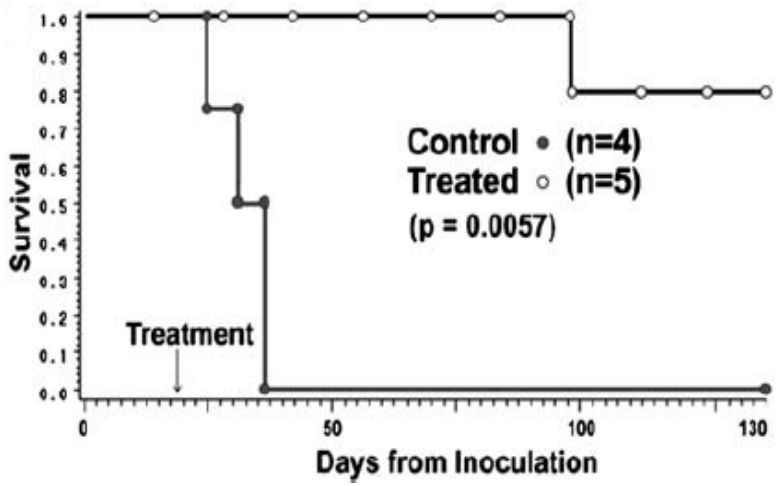
Source: Phillips, W. et al Advanced Drug Delivery Reviews 2014

RNL™ Preclinical Data

Performance in Animal Brain Cancer Models



RNL™ in orthotopic animal models of human brain cancer.



High doses of radiation that can be delivered by RNL™, significantly prolongs survival in these animal models.

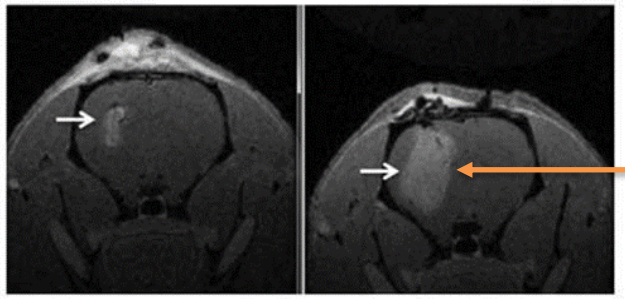
PLUS™ THERAPEUTICS

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

RNL™ Preclinical Data

Tumor Regression in Animal Brain Cancer Models

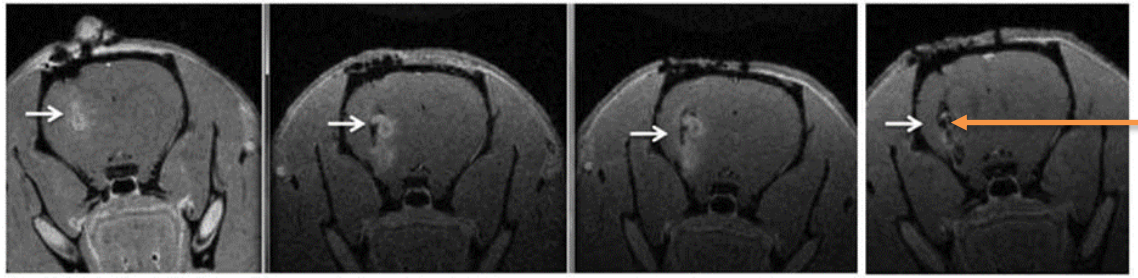
Control



Day -1 Day 14 Control

Tumor growth & expansion in untreated control animals with brain cancer.

RNL™ Treatment



Day -1 Day 14 Post-Tx Day 28 Post-Tx Day 70 Post-Tx

Tumor regression in RNL™ treated brain cancers.

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

RNL™ Fits Within Current Clinical Workflows

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



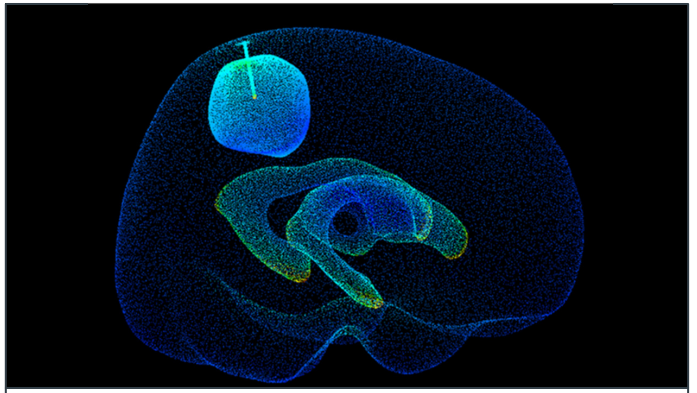
Preoperative targeting & surgical planning



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).
- No treatment-related SAEs observed.
- Early signals of efficacy in patients with adequate dosing and tumor coverage.
- Supported by a NIH/NCI grant through Phase 2.

ClinicalTrials.gov: NCT01906385

Phase 1 Dose Escalation Scheme

Cohort	Infused Volume (mL)	Total RNL™ Activity (mCi)	Concentration (mCi/mL)	Average Absorbed Dose (Gy)	Status
1	0.66	1.0	1.5	198	**First 6 cohorts complete** **(n = 18 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	TBD	
7	**13.2**	**31.2**	**2.5**	**TBD**	**Pending DSMB Meeting**

Tumor Coverage Implications

+ 8.8 mL treatment volume may cover ~3.5 cm diameter tumor plus a 0.5 cm margin
+ 13.2 mL treatment volume may cover ~4.0 cm diameter tumor plus a 0.5 cm margin

Safety Margin (continued)

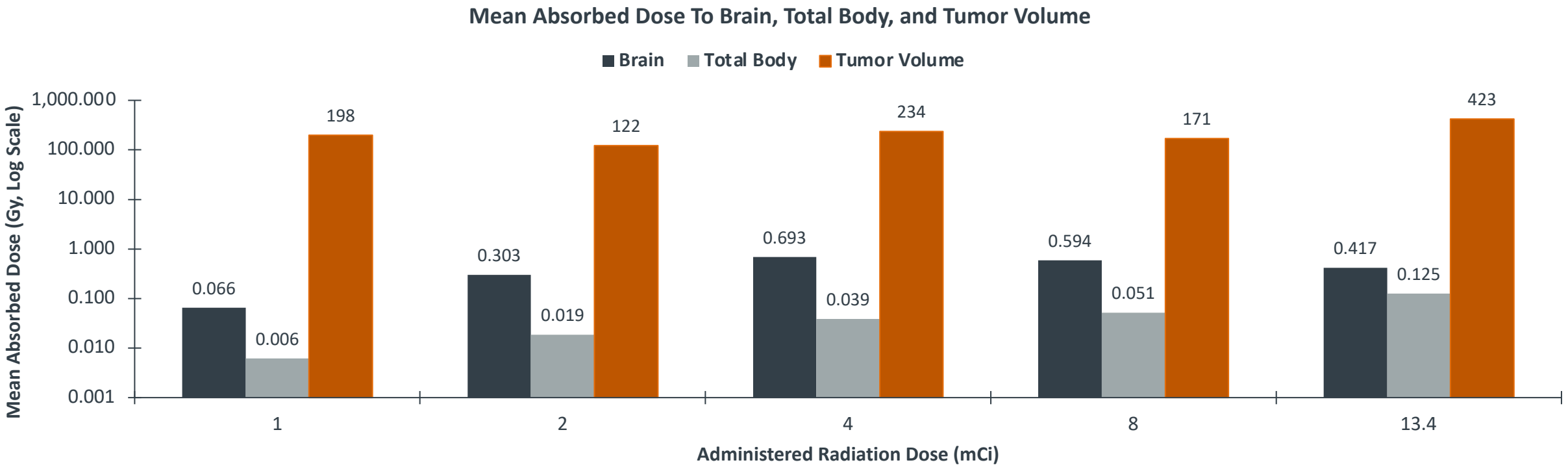
No SAE or AE Correlation with Increasing Doses

Adverse Event	Cohort 1		Cohort 2		Cohort 3		Cohort 4		Cohort 5		Total		Incidence
	n = 3		n = 3		n = 3		n = 3		n = 3		n = 15		
	G1/2	G3+	G1/2	G3+	G1/2	G3+	G1/2	G3+	G1/2	G3+	G1/2	G3+	
Fatigue	2		1				2		1		6		40%
Diarrhea	1		1		2						4		27%
Gait Abnormality			2		1				1		4		27%
Headache	1		2				1				4		27%
Hemiparesis	1		1		1		1				4		27%
Cerebral Edema				1	1					1	1	2	20%
Lightheadedness	1				2						3		20%
Scalp Discomfort	2		1								3		20%
Seizure	1			1				1			1	2	20%
Hyperglycemia (Diabetes)								2				2	13%
Weakness								2				2	13%
Leukocytosis								1				1	7%

- No treatment related SAEs
- Four SAEs were reported, none deemed causally related to RNL™
- Most AEs were causally unrelated to RNL™ except scalp discomfort, which was considered related to the surgical procedure

Safety Margin

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

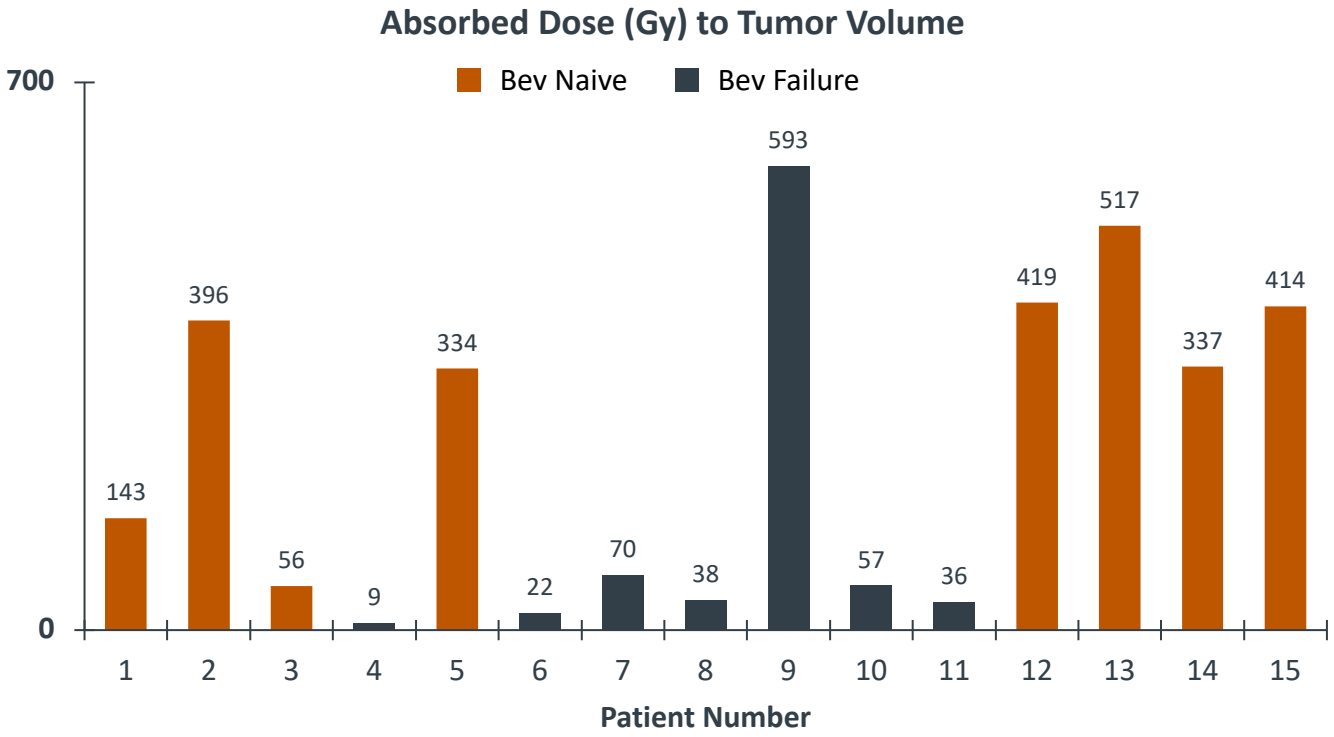


+ Mean total body absorbed dose (AD) ≤ 0.15 Gy and mean organ AD ≤ 0.70 Gy
+ Ratio of mean tumor volume AD/mean total body AD in cohorts 4 & 5, ≥ 3,000

Absorbed Dose Through Cohort 5

Dosing Volume and Convection Effect

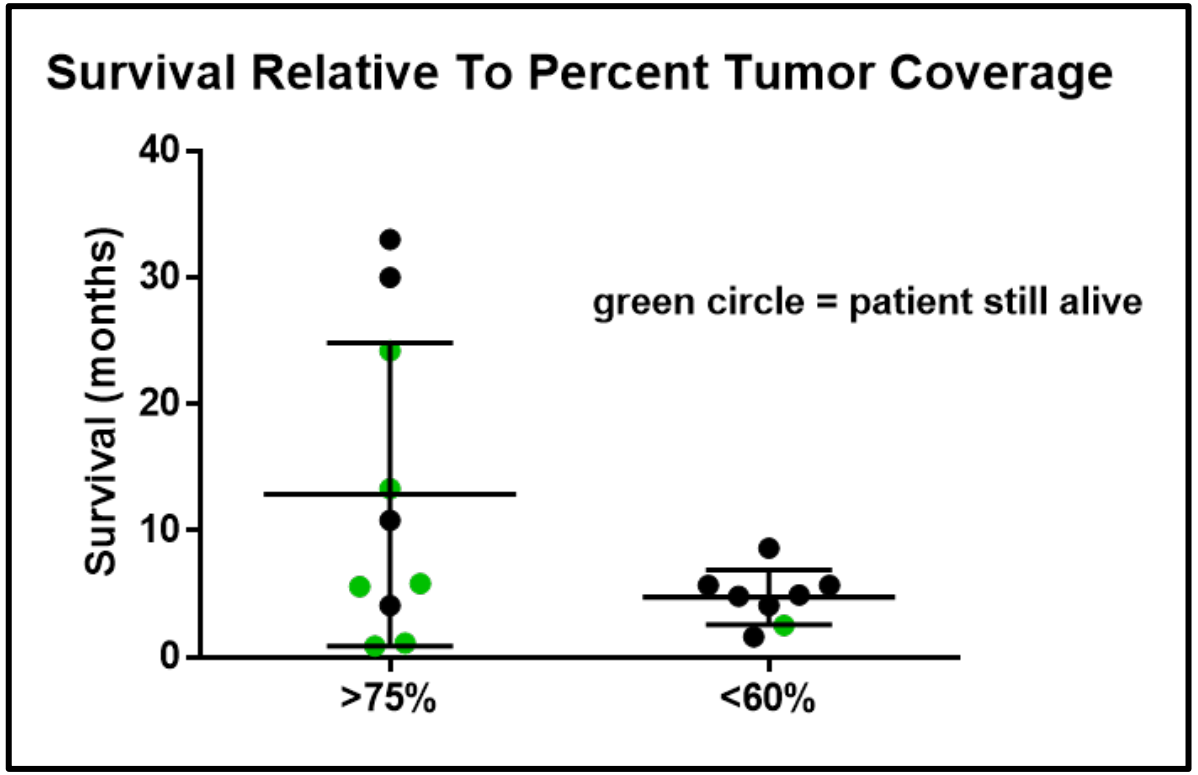
- Absorbed Dose (Gy) to Tumor Volume
  - Maximum: 593 Gy
  - All 15 Patients: median 143 Gy (range 9-593 Gy)
  - 8 Bev Naïve Patients: median 367 Gy (range 56-517 Gy)
  - 7 Bev Failure Patients: median 38 Gy (range 9-593 Gy)
- Patients with poor AD/TV due to poor convection were disproportionately patients failing bevacizumab



Impact on Survival

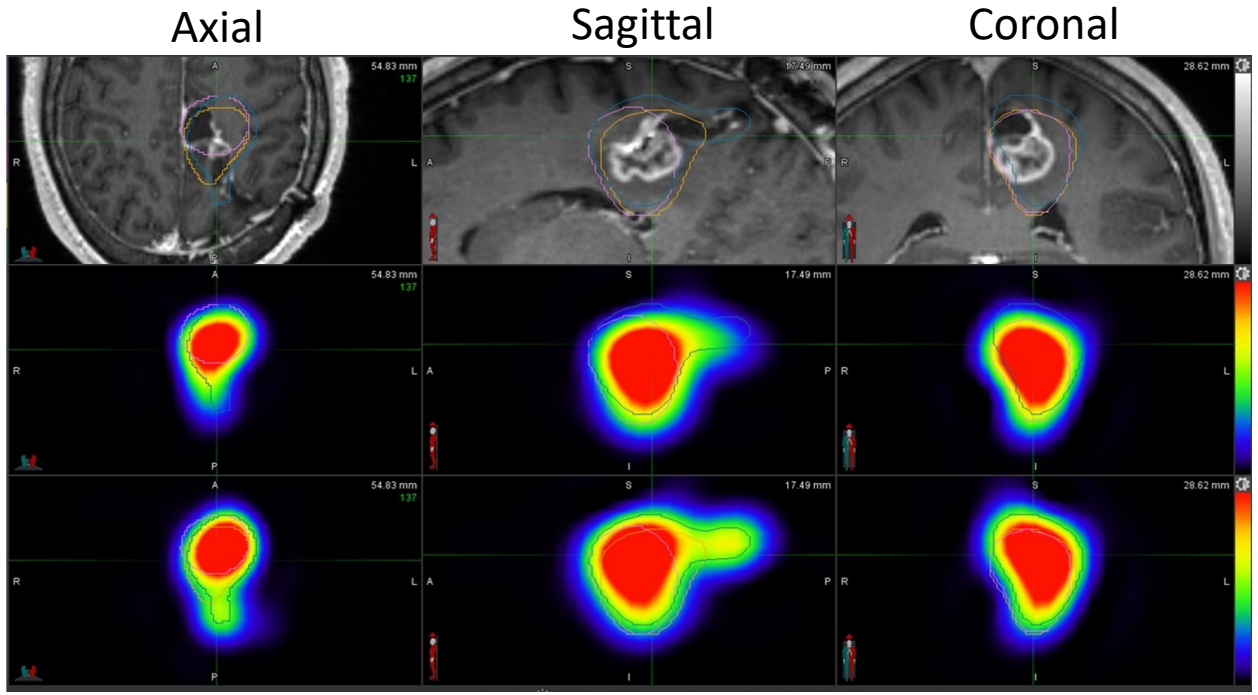
Correlation with Tumor Coverage Through Cohort 6

- 2 long term survivors greater than 30 months.
- Median and mean survival duration in subjects with tumor coverage > 75% (n=10) currently 8.3 months (range 0.9 – 33) and 12.9 months (95% CI 4.3 – 21.5), respectively, 6 patients still alive.
- Median survival duration with tumor coverage < 60% (n=8) is 4.9 months , 1 patient still alive.



Tumor Coverage and Retention

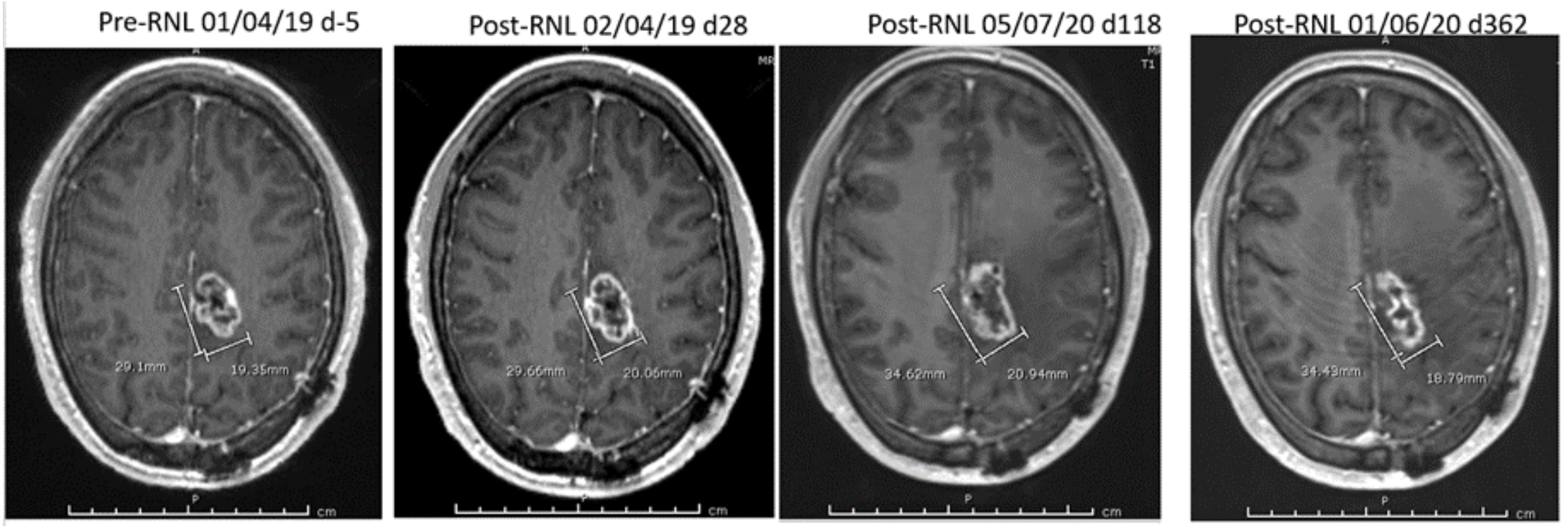
Subject 01-014



- 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™

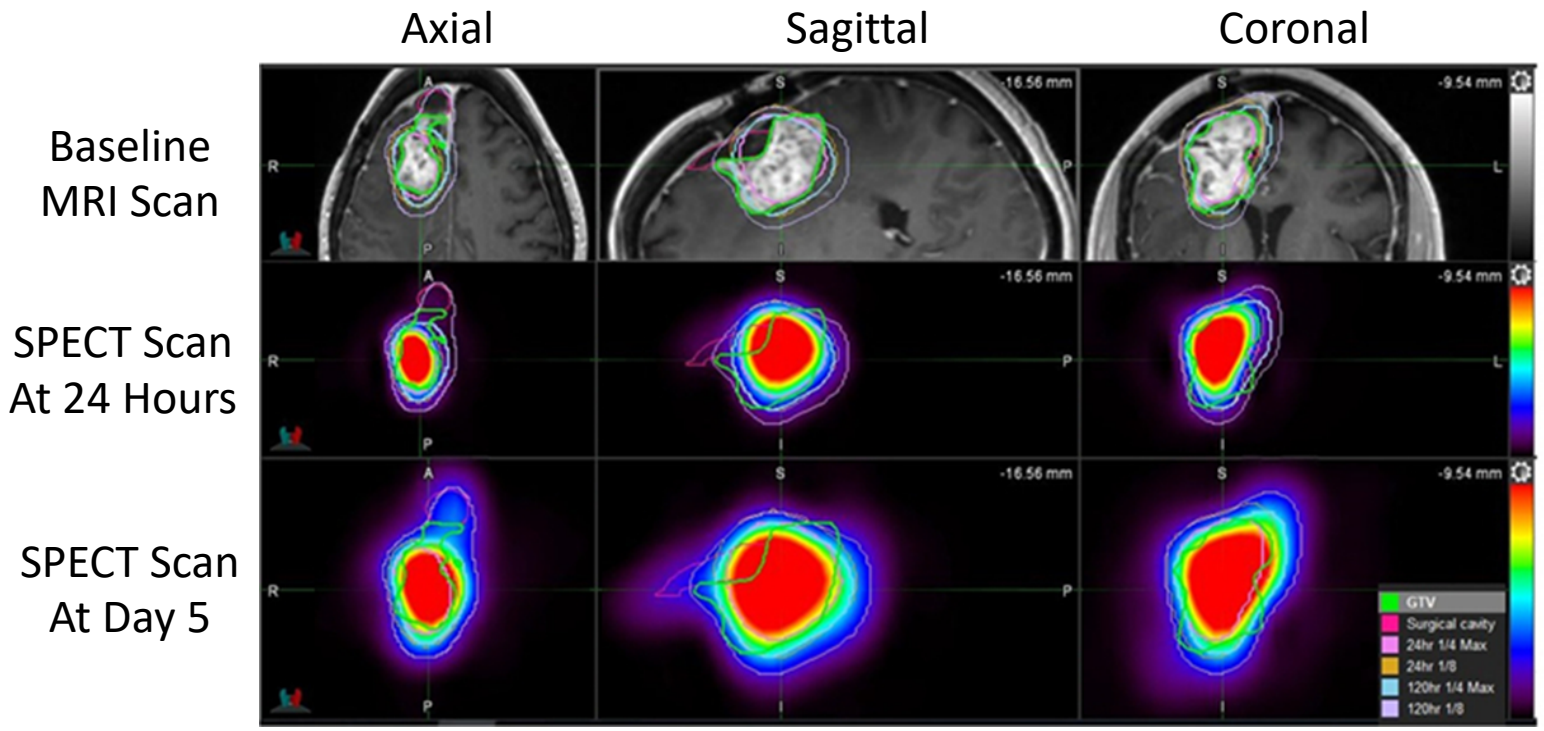
Subject 01-014: Tumor Response Observed to Day 362



- 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 (>600 days)

Tumor Coverage and Retention

Subject 01-017

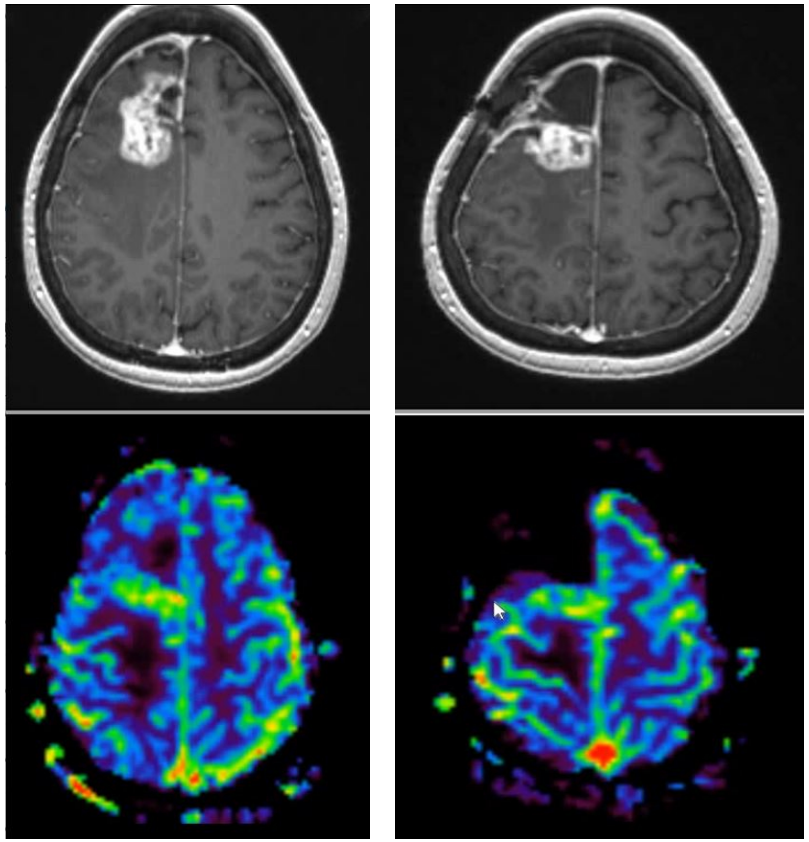


- Tumor volume was 18.8 mL and tumor coverage was 87%
- Absorbed dose delivered to tumor was 336 Gy

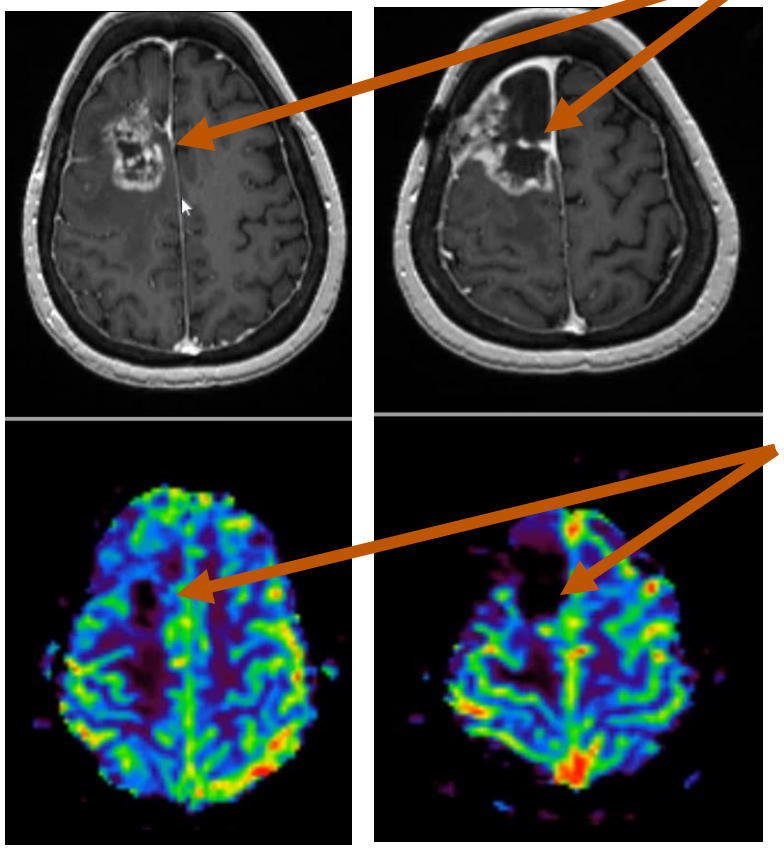
MRI & Perfusion Imaging

Subject 01-017: Tumor Ablation & Loss of Perfusion

Pre-Treatment



Day 56



RNL™ Development Plan

Recurrent Glioblastoma	2021	2022	2023	2024	2025
ReSPECT™ Pilot/Phase 1 for rGBM					
Manufacturing & Commercial Scale Up					
Anticipated Pivotal for rGBM					

LMC & Pediatric Brain Cancer	2021	2022	2023	2024	2025
FDA IND Meeting for LMC					
Pilot/Phase 1 for LMC					
FDA IND Meeting for Pediatric Brain Cancer					
Pilot/Phase 1 for Pediatric Brain Cancer					

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RNL™ Indication Expansion

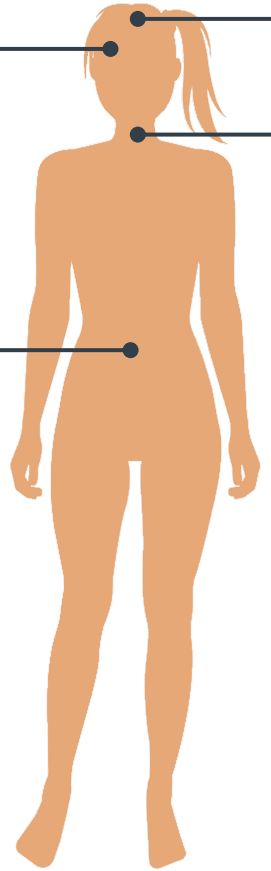
Opportunity to Address Significant Unmet Needs for Multiple Rare Cancers

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

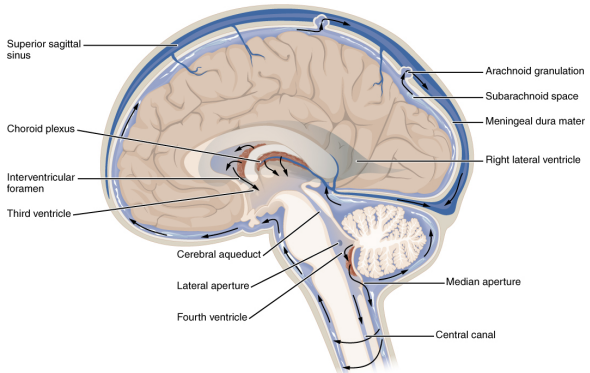
* High Grade Glioma, Ependymoma, Diffuse Intrinsic Pontine Glioma

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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.

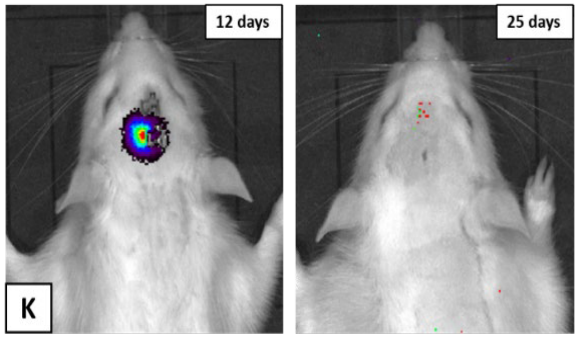


100 nm NanoLiposomes in CSF

+ 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

+ RNL™ efficacy in 2 cohorts (n=8) of animals induced with LC; 1 cohort treated with RNL (0.69 mCi) and 1 cohort served as a control and injected with empty nanoliposomes.
+ Specifically, 62.5% of animals injected with RNL™ had a decrease in tumor size.



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https://cnx.org/contents/FPtK1zmh@8.25:fEI3C8Ot@10/Preface

Source: NatureRes (2019) 9:12587

Source: internal data, manuscript in preparation

RNL™ Development Plan

Recurrent Glioblastoma	2021	2022	2023	2024	2025
ReSPECT™ Pilot/Phase 1 for rGBM					
Manufacturing & Commercial Scale Up					
Anticipated Pivotal for rGBM					

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FDA IND Meeting for LMC					
Pilot/Phase 1 for LMC					
FDA IND Meeting for Pediatric Brain Cancer					
Pilot/Phase 1 for Pediatric Brain Cancer					

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Forthcoming Milestones for 2021

- Complete enrollment & report data from U.S. ReSPECT™ trial for RNL™ in recurrent GBM
- Complete CMC activities for RNL™
- Complete Phase 2/pivotal trial planning with FDA
- IND-enabling studies if needed, for follow-on RNL™ indications
- Move RNL™ into Phase I for leptomeningeal cancer & pediatric brain cancer
- Complete additional preclinical studies for RNL™ and DRNL™
- Potential acquisition, in-license new drug development candidates
- Partner RNL™, DocePLUS™ & DoxoPLUS™ assets

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Capitalization Summary

Select Data (as of 09/30/20)	
Cash	$7.6M
Common Shares Outstanding	4,591,415
Series U warrants	3,045,000
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