

Corporate Presentation

January 2021

PLUS™ THERAPEUTICS

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: A CNS Oncology Company

- 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



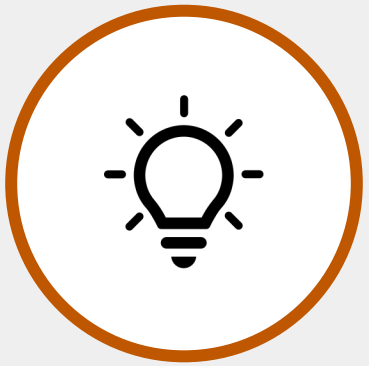
- Meningioma (38%)
- Pituitary (17%)
- Glioblastoma (15%)
- Other Non-Glioma (11%)
- Other Glioma (11%)
- Nerve Sheath (9%)

Sources: CBTRUS Statistical Report, NBTS

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PLUS Therapeutics: Snapshot

Committed to developing novel, targeted therapies for rare and difficult to treat CNS cancers



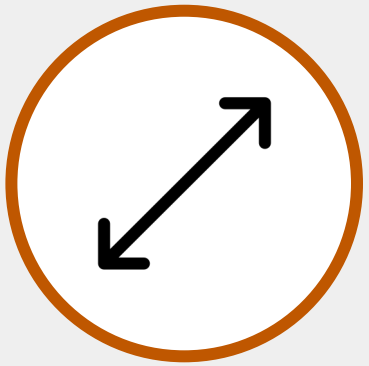
Proprietary and versatile nanoscale drug delivery platform.



Expanding pipeline now with 4 investigational, 3 clinical stage drugs all intended to improve patient survival and quality of life.



Lead investigational drug, Rhenium NanoLiposome (RNL™) is a novel radiotherapy being evaluated in a NIH-funded clinical trial for recurrent brain cancer.



Intend to expand RNL™ into the clinic for additional CNS and rare oncology indications with unmet medical needs.

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Drug Development Pipeline

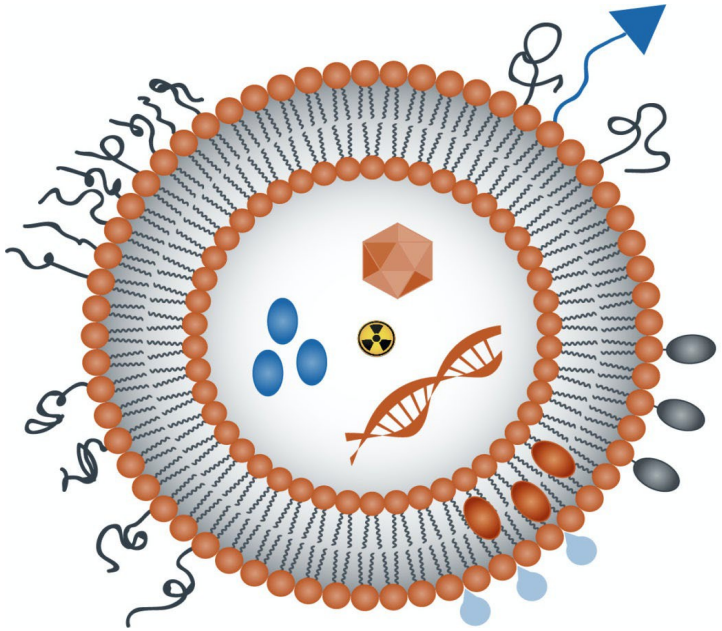
INVESTIGATIONAL DRUG	INDICATION	REGULATORY DESIGNATION	DEVELOPMENT STAGE	3rd PARTY FUNDING
RNL™ BMEDA-Chelated Rhenium NanoLiposome*	Recurrent Glioblastoma	FDA Orphan Drug FDA Fast Track	U.S. Phase 1- Enrolling	NIH/NCI
	Leptomeningeal Cancer		IND submitted Q1 2021	
	Various Pediatric CNS Cancers		IND submitted Q1 2021	
DoxoRNL™ BMEDA-Chelated Rhenium NanoLiposome/Liposomal Doxorubicin*	Various Cancers		Preclinical	
DocePLUS™ Albumin-Stabilized PEGylated Liposomal Docetaxel*	Various Cancers	FDA Orphan Drug	U.S. Phase 1- Complete, Published	
DoxoPLUS™ PEGylated Liposomal Doxorubicin**	Various Cancers		Clinical Bioequivalence-Complete, Published	

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* proprietary, innovative ** complex generic

Nanoscale Drug Development Capability & Technology

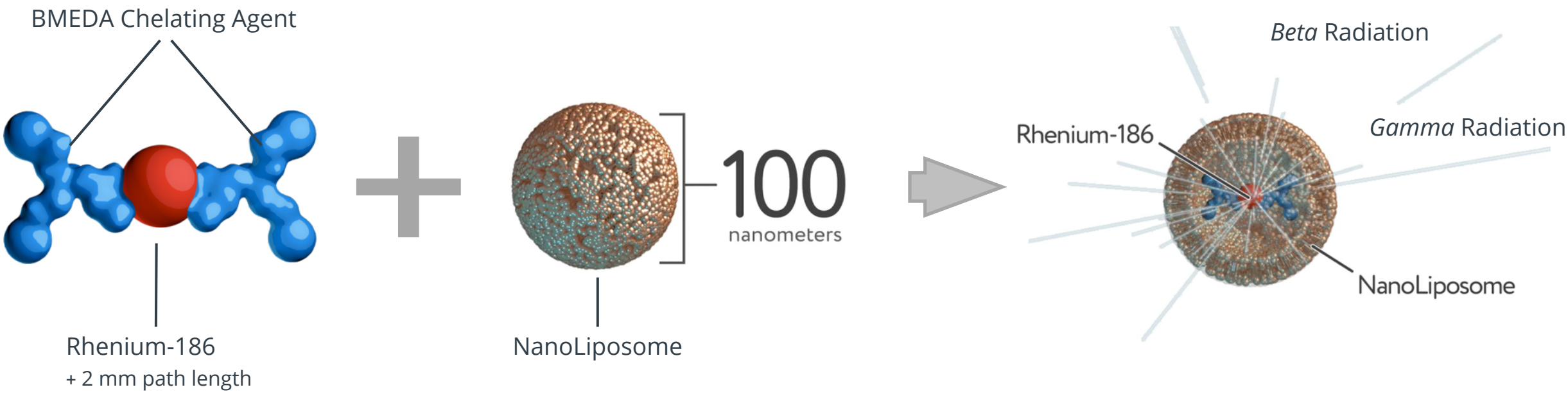
- Drug encapsulation
- Diverse compound loading (radionuclides, cytotoxics)
- Protein membrane stabilization technology
- Manufacturing & scale up
- Multiple FDA IND approvals & completed clinical trials
- Commercial manufacturing facility



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Lead Asset: Rhenium NanoLiposome (RNL™) for GBM

Proprietary Radiotherapy Infused Directly Into Tumor Via Convection Enhanced Delivery



Rhenium NanoLiposome™

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Glioblastoma

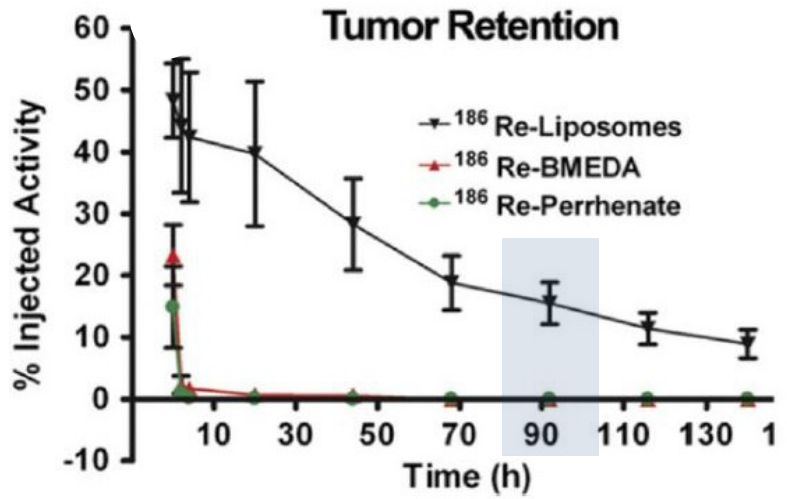
A rare, incurable, and fatal brain cancer with no good treatment options



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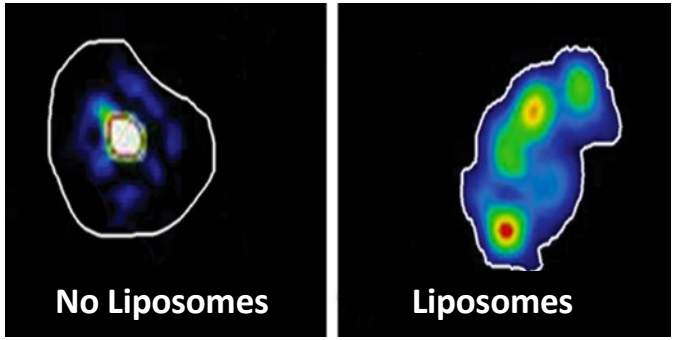
RNL™ Prolonged Tumor Half-life and Brain Retention

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



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

Tumor Dispersion

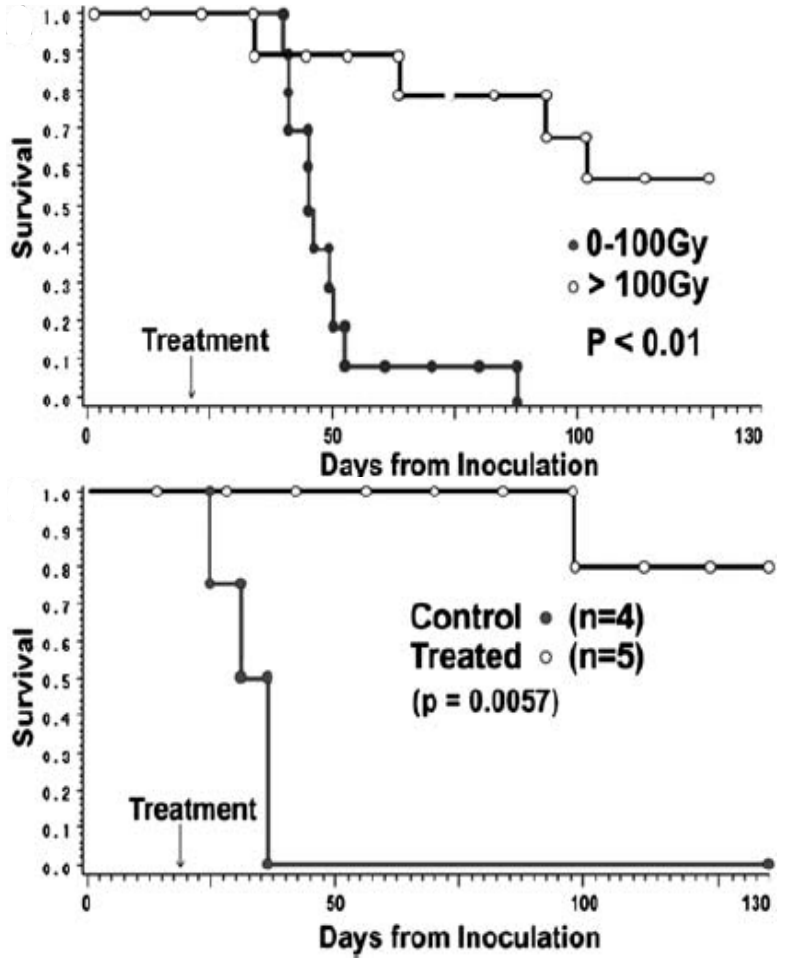


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Source: Phillips, W. et al Advanced Drug Delivery Reviews 2014

RNL™ Preclinical Performance in Animal Brain Cancer Models

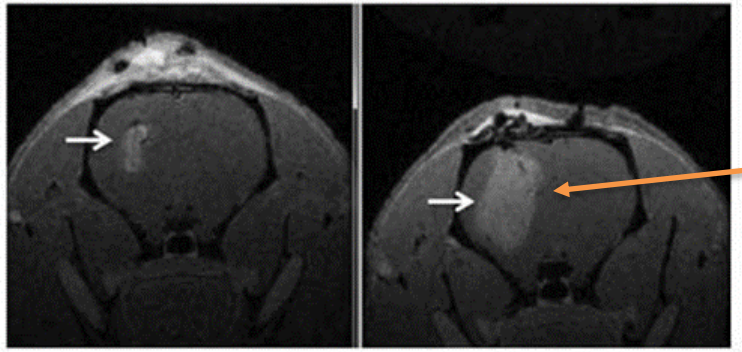
- RNL™ in orthotopic animal models of human brain cancer.
- High doses of radiation that can be delivered by RNL™, significantly prolongs survival in these animal models.



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

RNL™ Tumor Regression in Preclinical Animal Models of Brain Cancer

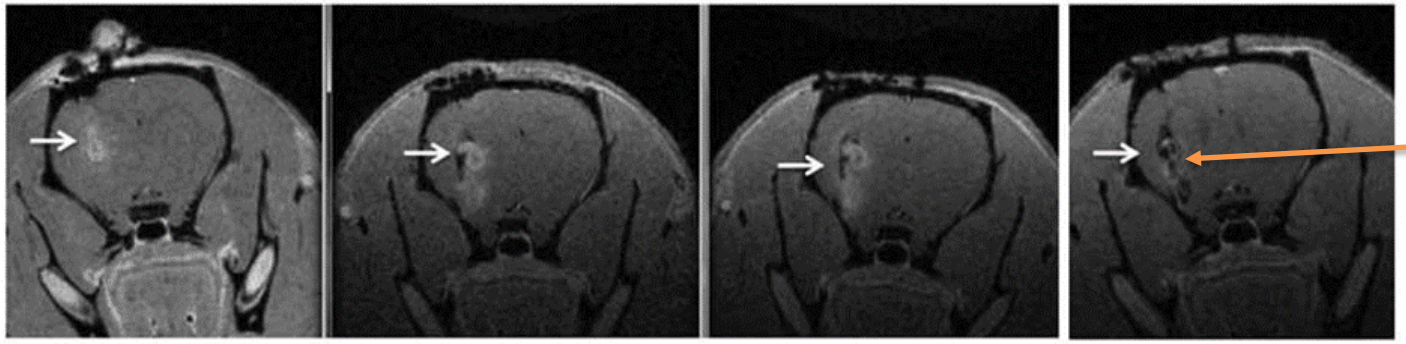
Control



Day -1 Day 14 Control

Tumor growth & expansion in un-treated control animals with brain cancer.

^{186}Re-Liposome Treatment



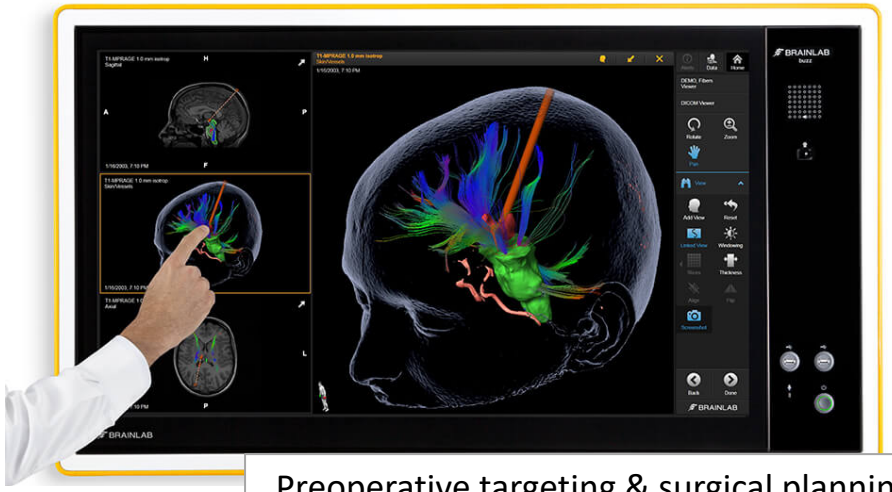
Day -1 Day 14 Post-Tx Day 28 Post-Tx Day 70 Post-Tx

Tumor regression in RNL™ treated brain cancers.

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

RNL™ Therapy Leverages Recent Advances in Information Technology, Imaging, Neurosurgery & Drug Delivery



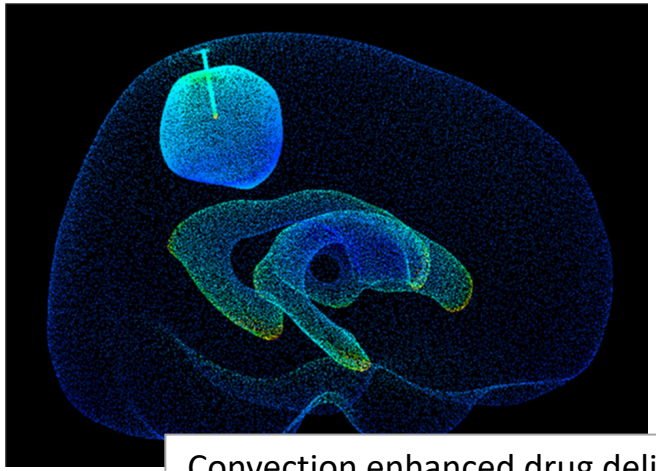
Preoperative targeting & surgical planning



Modern neurosurgical operating theater



Stereotactic catheter placement



Convection enhanced drug delivery

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Images Coutesy Brainlabs
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.

Product / Technology

Potential Advantages of Rhenium NanoLipsome Compared to External Beam Radiation Therapy



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RNL™ Phase 1/2 Clinical Trial Design

ReSPECT CLINICAL TRIALS

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.

NIH National Institutes of Health

UT Health San Antonio
The University of Texas Health Science Center at San Antonio

UT Southwestern Medical Center®

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

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ClinicalTrials.gov: NCT01906385

ReSPECT™ 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

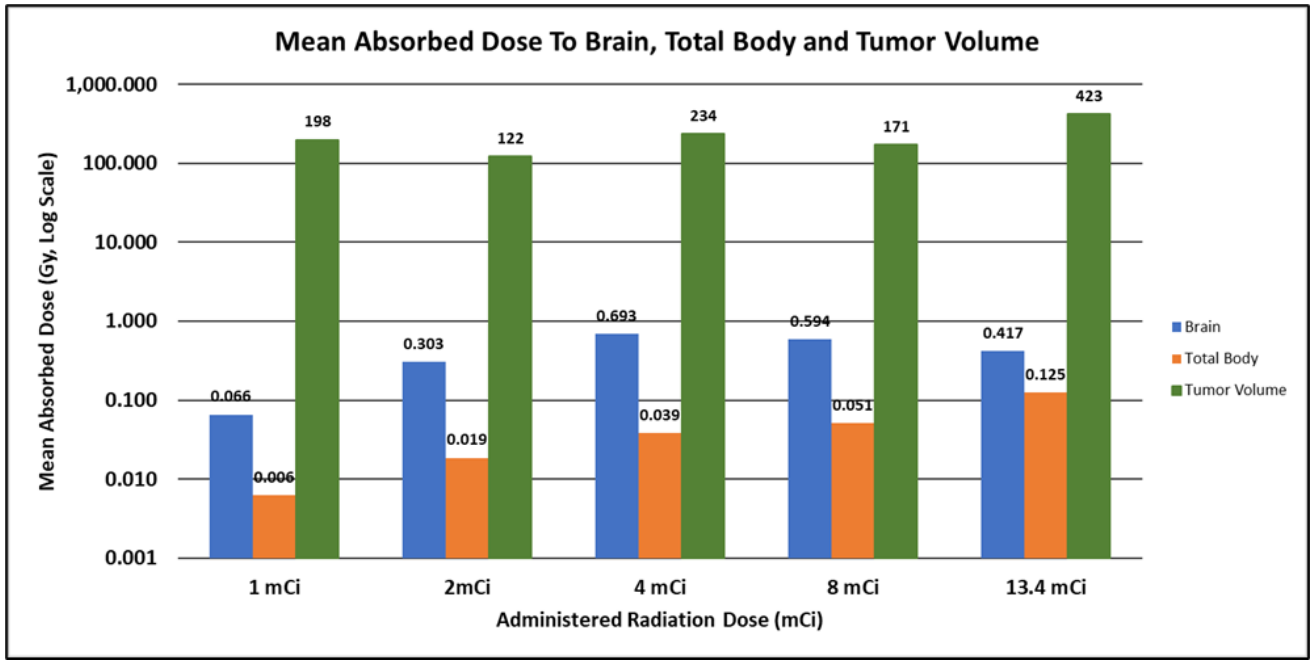
+ 8.8 mL treatment volume may cover ~3.5 cm diameter tumor plus a 0.5 cm margin
+ 13.2mL treatment volume may cover ~4.0 cm diameter tumor plus a 0.5 cm margin

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RNL™ Safety Margin

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

- Mean total body absorbed dose (AD) ≤ 0.15 Gy
- Mean organ AD ≤ 0.70 Gy
- The ratio of mean tumor volume AD to mean total body AD in cohorts 4 & 5, ≥ 3,000



RNL™ Safety Margin

No SAE or AE Correlation with Increasing Doses Of RNL™

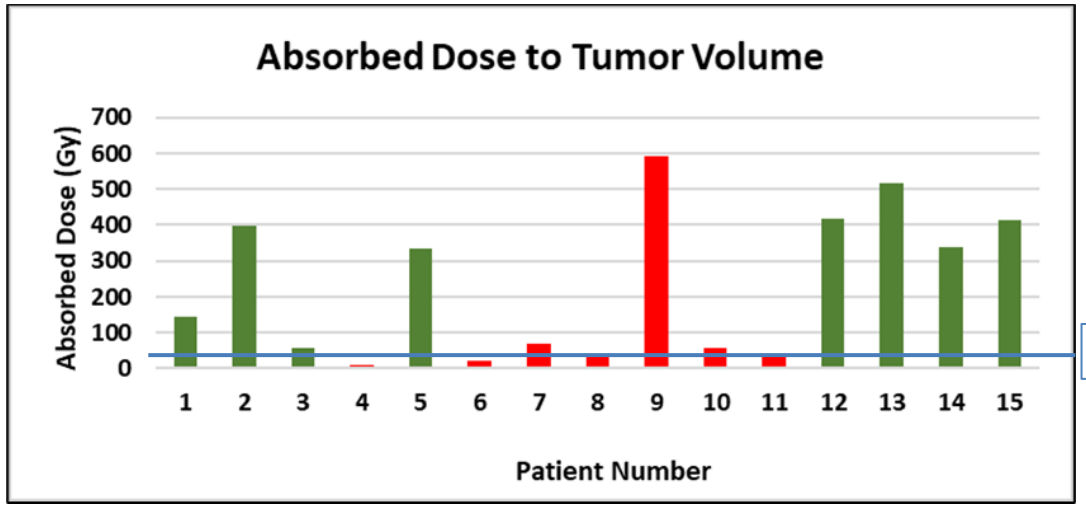
- No treatment related SAEs.
- Four Serious Adverse Events (SAEs) were reported, none deemed causally related to RNL™.
- Most adverse events (AEs) were causally unrelated to RNL™ except scalp discomfort, which was considered related to the surgical procedure.
- The AEs with the highest incidence were: Fatigue (40%), Diarrhea (27%), Gait Abnormality (27%), Headache (27%), Hemiparesis (27%), Lightheadedness (20%), Scalp Discomfort (20%), Seizure (20%) and Cerebral Edema (20%).

Adverse Event	Cohort 1 n = 3		Cohort 2 n = 3		Cohort 3 n = 3		Cohort 4 n = 3		Cohort 5 n = 3		Total 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	
Diarrhea	1		1		2						4	
Gait Abnormality			2		1				1		4	
Headache	1		2				1				4	
Hemiparesis	1		1		1		1				4	
Cerebral Edema				1	1					1	1	2
Lightheadedness	1				2						3	
Scalp Discomfort	2		1								3	
Seizure	1			1				1			1	2
Hyperglycemia (Diabetes)								2				2
Weakness								2				2
Leukocytosis								1				1

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Absorbed Dose Through Cohort 5: Dosing Volume & Bevacizumab Effect

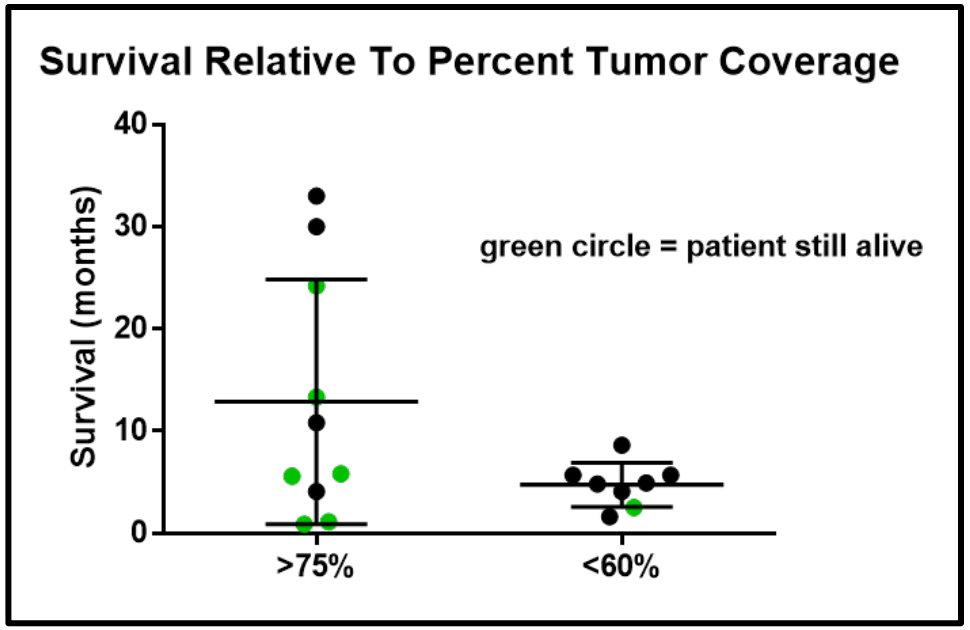
- The maximum absorbed dose to the tumor volume was 593 Gy.
- Median absorbed dose (AD) to tumor volume across 15 subjects - 143 Gy (range 9 – 593).
- Median AD in 8 bevacizumab-naïve subjects was 367 Gy (range 56 – 517).
- Median AD in 7 subjects failing bevacizumab-38 Gy (range 9 – 593).
- Prior administration of bevacizumab appears to negatively impact convection.



Impact of RNL™ 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.

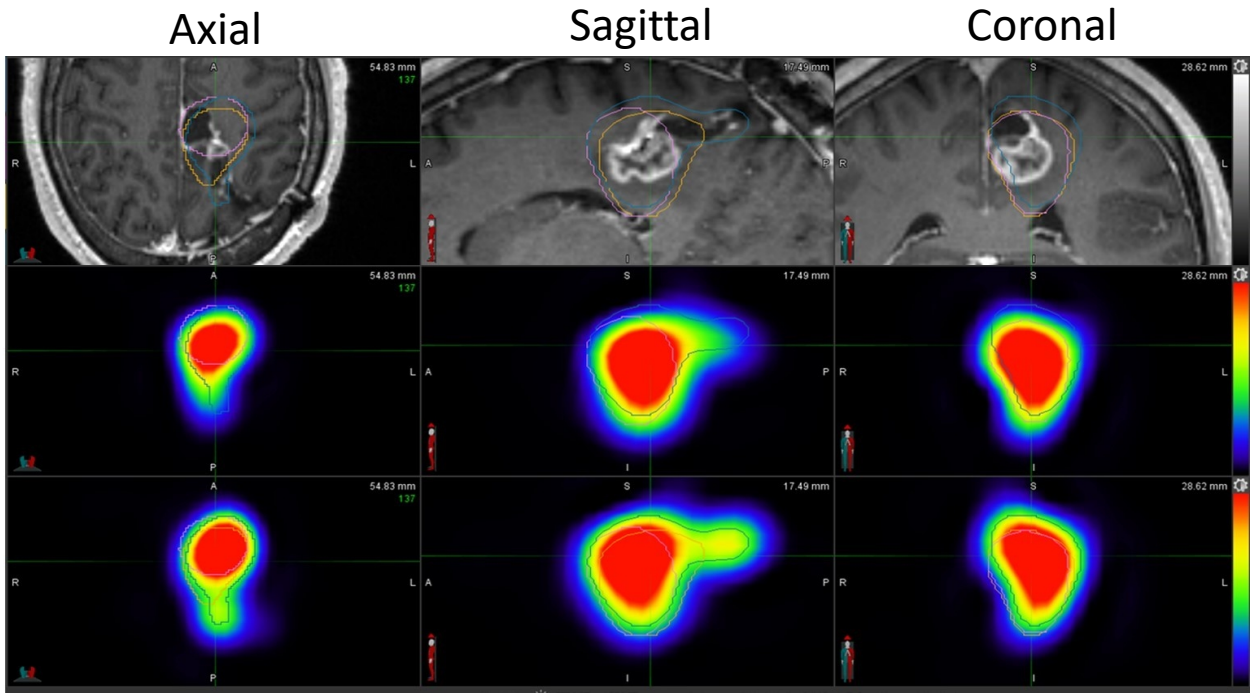


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Tumor Coverage and Retention

Subject 01-014

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

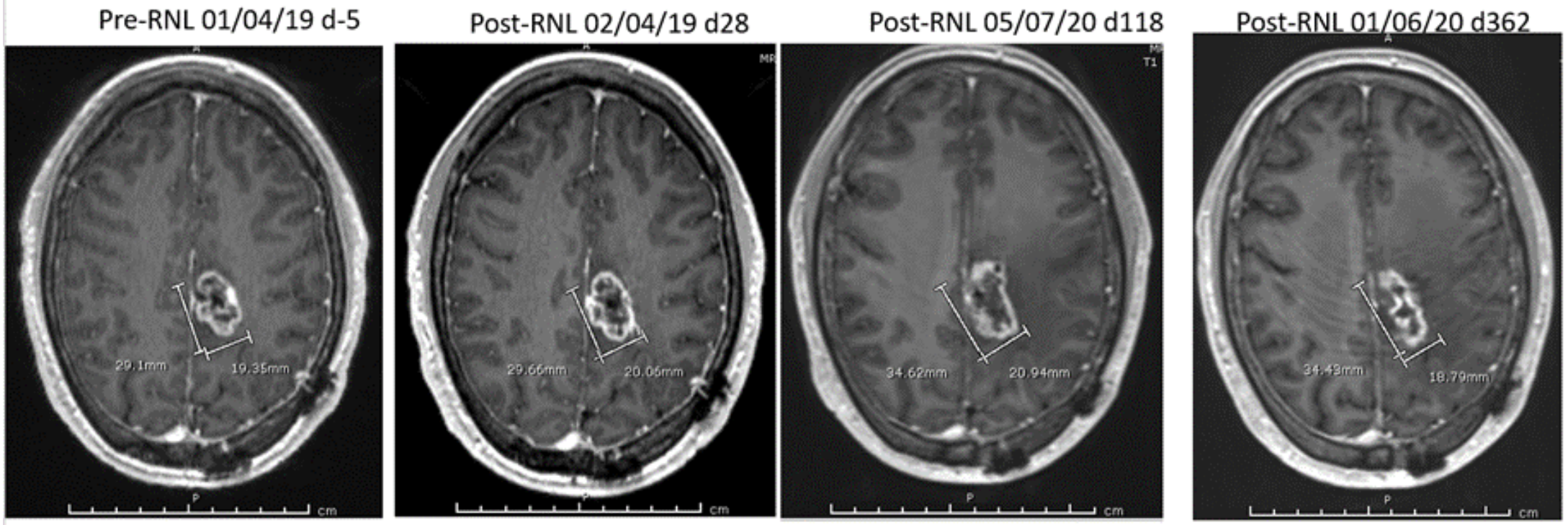


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Natural History of Recurrent GBM Lesions after RNL™

Tumor Response Observed To Day 362

Subject 01-014



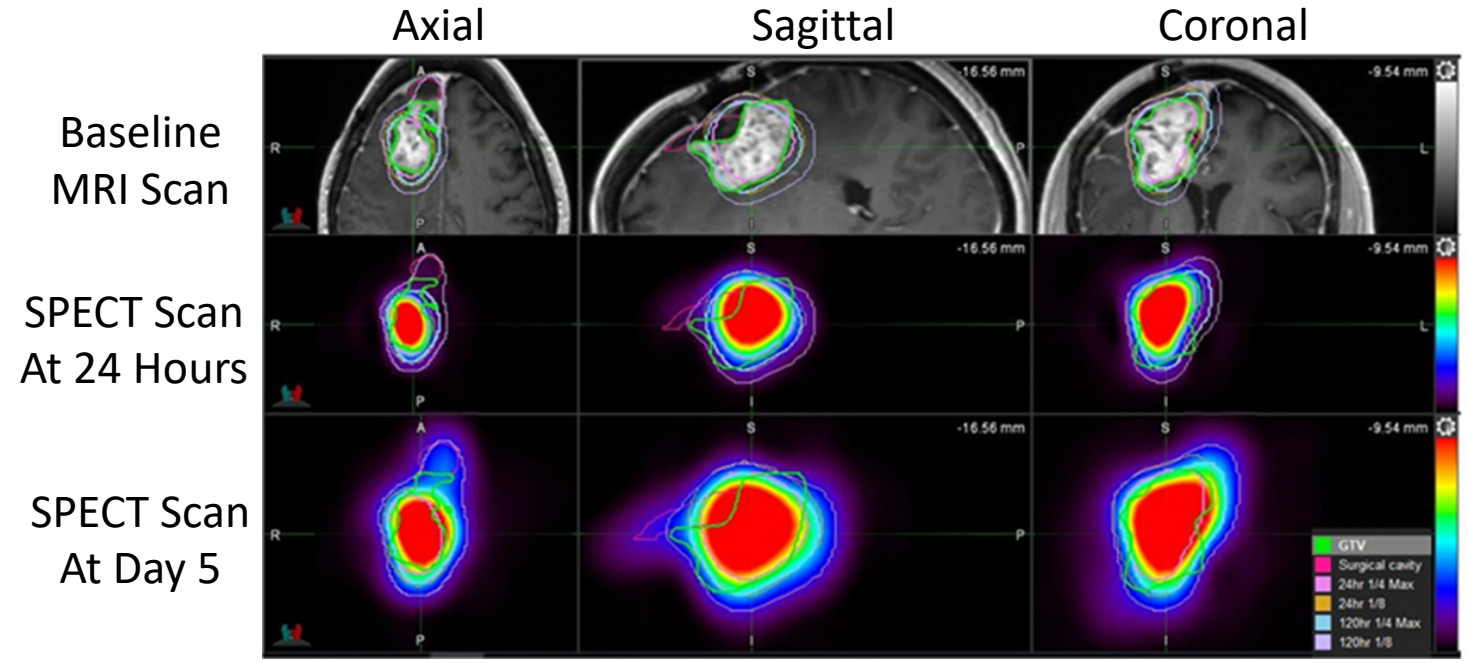
- MRI scans revealed an initial increase in size which peaked at Day 118, with some associated edema, followed by tumor shrinkage out to at least Day 362
- Patient remains alive (>600 days)

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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



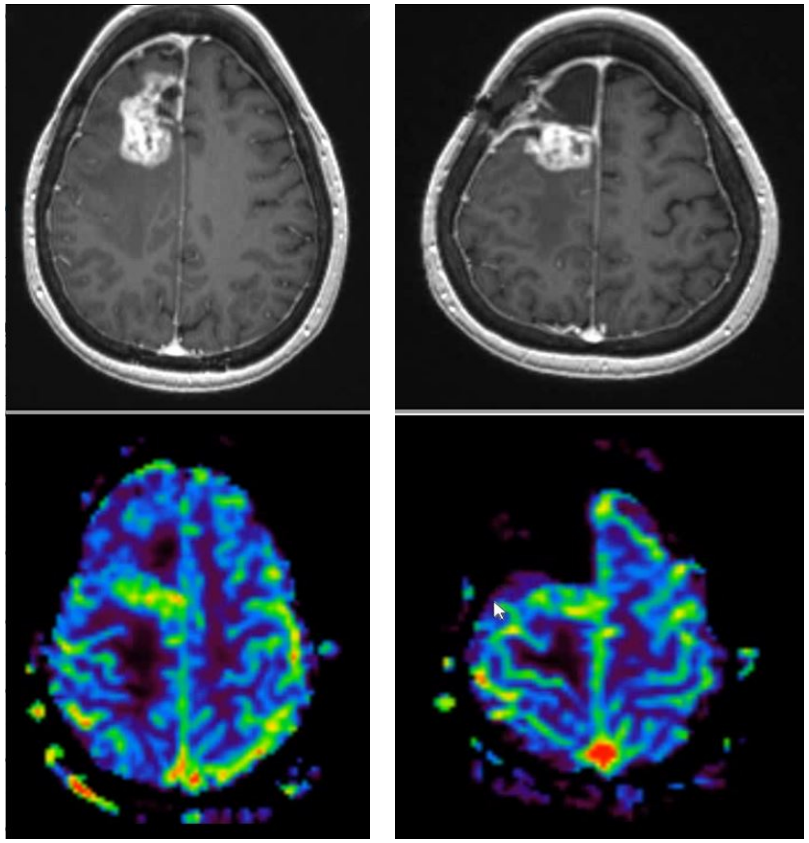
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MRI & Perfusion Imaging

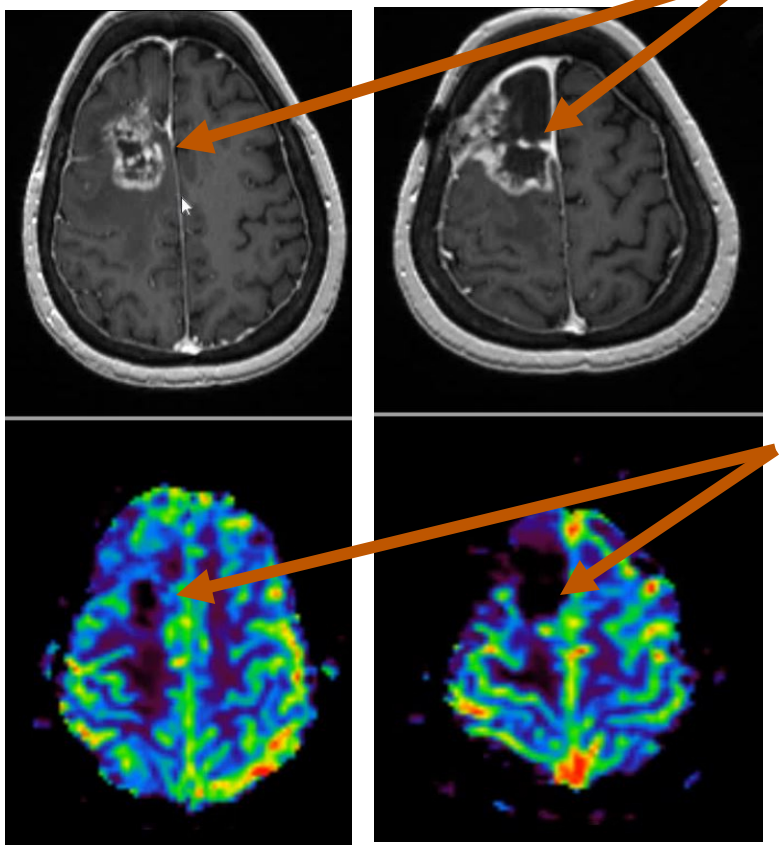
Tumor Ablation & Loss of Perfusion

Subject 01-017

Pre-Treatment



Day 56



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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					

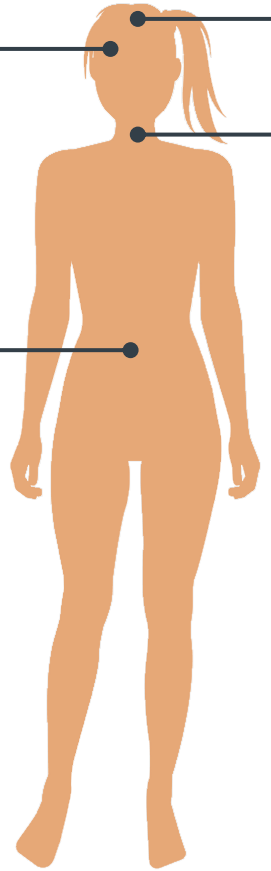
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RNL™ Indication Expansion

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

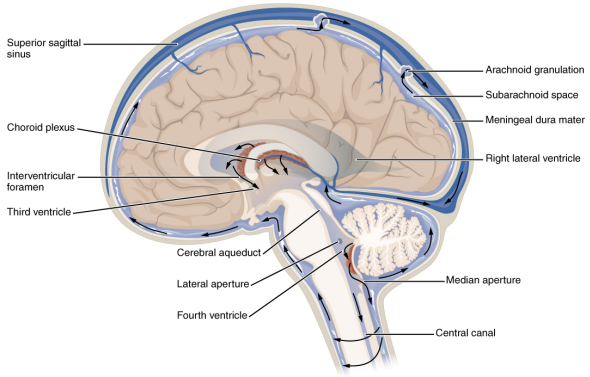
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* High Grade Glioma, Ependymoma, Diffuse Intrinsic Pontine Glioma

Therapeutic Rationale for Use of RNL™ for Leptomeningeal Cancer (LMC)

Leptomeningeal cancer

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.



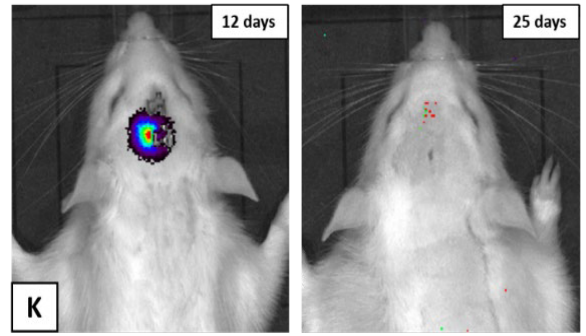
Nanoparticles in CSF

Nanoparticles of ~ 100nm:

+ 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.

RNL™ in LMC

Preclinical- 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: internaldata, 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					

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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Out-Licensing Pipeline

Patented DocePLUS™ (NanoLiposomal Docetaxel)

- Next-generation formulation of TAXOTERE® (docetaxel)
  - 3 key design changes
  - Eliminates need for pre-medications to reduce hypersensitivity reactions
- Published U.S. 29-patient, single-center Phase 1 clinical trial in solid tumors
  - Better tolerated than TAXOTERE®
  - Improved efficacy with increasing doses without a concomitant increase in toxicity
- Opportunities beyond TAXOTERE® labeled indications
  - KOLs and payers recommended targeting SCLC, Pancreatic, TNBC
  - Peak potential annual U.S. sales > $760M
- U.S. FDA
  - Orphan drug designation received for SCLC
  - Pre-IND feedback confirmed 505(b)(2) pathway and outlined Phase 2 clinical trial design

Generic DoxoPLUS™ (NanoLiposomal Doxorubicin)

- Generic formulation of CAELYX® and LIPODOX®
  - Designed to treat breast cancer, ovarian cancer, multiple myeloma, Kaposi's sarcoma
  - Estimated E.U. and U.S. combined market size - $250M
- Bioequivalence clinical study completed versus CAELYX® in accordance with European Medicines Agency guidelines
- U.S. FDA IND is approved to conduct a bioequivalence clinical study versus LIPODOX®

Interested in partnering both assets

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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 DoxoRNL
- 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