

ReSPECT™ Phase 1 Trial in Recurrent Glioblastoma: Interim Report

November 19, 2020

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Forward-Looking Statements

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Introduction and Agenda

Marc Hedrick, M.D.

President and Chief Executive Officer

Plus Therapeutics

Today's Agenda

- Introduction
- Recurrent glioblastoma – disease background
- Investigational drug: Rhenium NanoLiposomes (RNL)
- ReSPECT Phase 1 trial – interim report
- Patient experience and perspective
- Q&A

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Presenters

Marc Hedrick, M.D.
President and Chief Executive Officer, Plus Therapeutics

Gregory Stein, M.D., M.B.A.
Senior Vice President, Clinical Development, Plus Therapeutics

Andrew J. Brenner, M.D., Ph.D.
Associate Professor of Medicine, Neurology, and Neurosurgery
The University of Texas, Health Services Center at San Antonio

Phyllis M.
ReSPECT Clinical Trial Patient

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We believe in the critical importance of discovering, developing, and delivering complex and innovative treatments for patients battling rare cancers.



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Company Highlights

+ Publicly traded on Nasdaq: PSTV

+ Proprietary nanoparticle drug development platform

+ Three clinical-stage oncology drugs in development

+ Lead drug funded by U. S. NIH/National Cancer Institute

+ Capital efficient, virtual drug development model

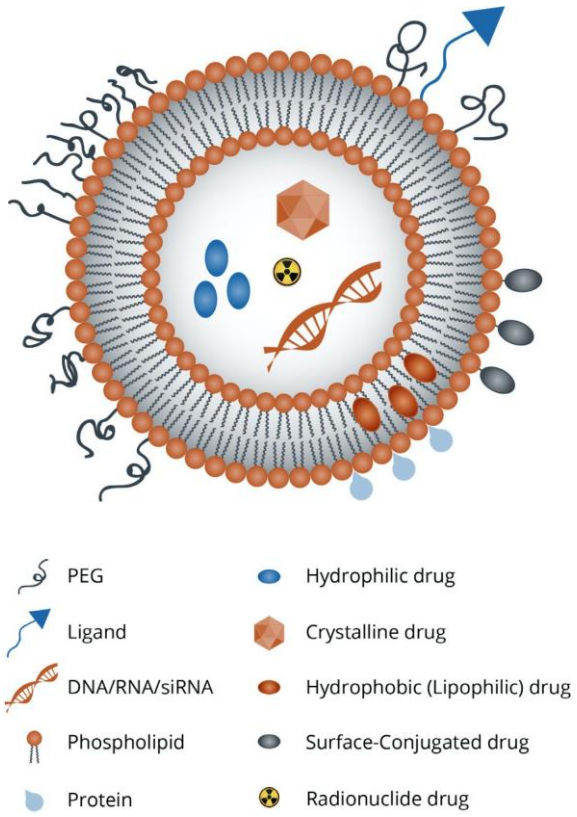
+ Corporate headquarters: Austin, Texas

+ Operations: San Antonio, Texas

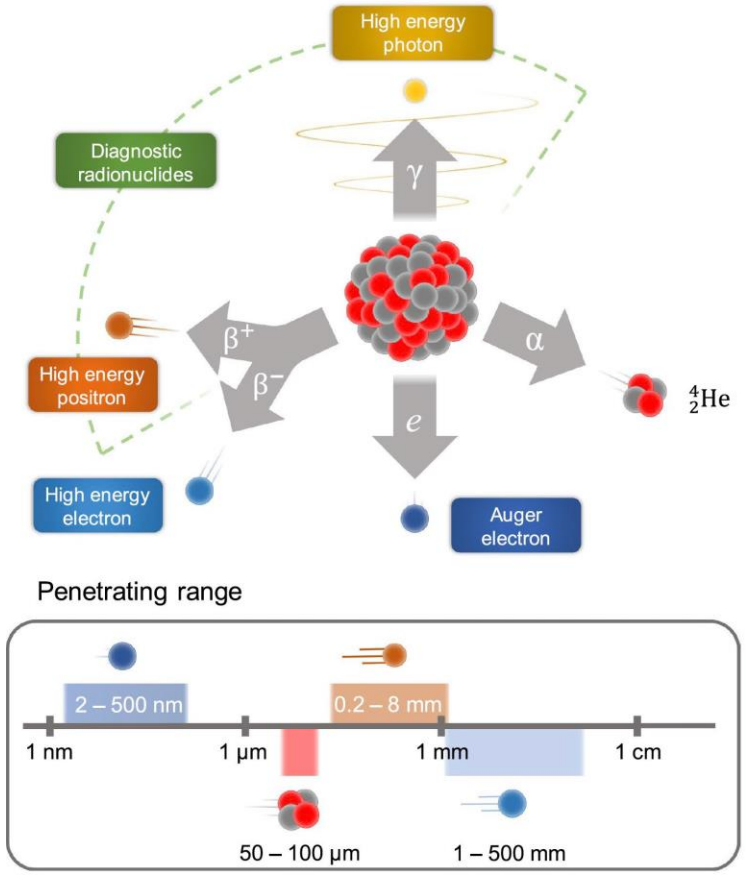
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Technology Platform

Nanoparticle Design & Manufacturing



Radionuclide Encapsulation & Delivery



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Drug Development Pipeline

RADIOTHERAPEUTIC PROGRAM	INDICATION	DELIVERY	DESIGNATION	FUNDING	DEVELOPMENT STAGE
RNL™ Rhenium-186 NanoLiposome*	Recurrent Glioblastoma	Intratumoral	FDA Orphan Drug/ Fast Track	NIH/NCI	U.S. Phase 1 Clinical Enrolling
	Leptomeningeal Carcinomatosis	Intrathecal or Intracerebroventricular	-	-	Late-stage Preclinical
	Peritoneal Carcinomatosis	Intraperitoneal	-	-	Late-stage Preclinical
	Head & Neck Squamous Cell Carcinoma	Intratumoral	-	-	Late-stage Preclinical

CHEMOTHERAPEUTIC PROGRAM	INDICATION	DELIVERY	DESIGNATION	FUNDING	DEVELOPMENT STAGE
DocePLUS™ Albumin-Stabilized PEGylated Liposomal Docetaxel*	Solid Tumor; Small Cell Lung Cancer	Intravenous	FDA Orphan Drug	-	U.S. Phase 1 Clinical Published
DoxoPLUS™ PEGylated Liposomal Doxorubicin**	Breast Cancer; Ovarian Cancer	Intravenous	-	-	Clinical Bioequivalence Published

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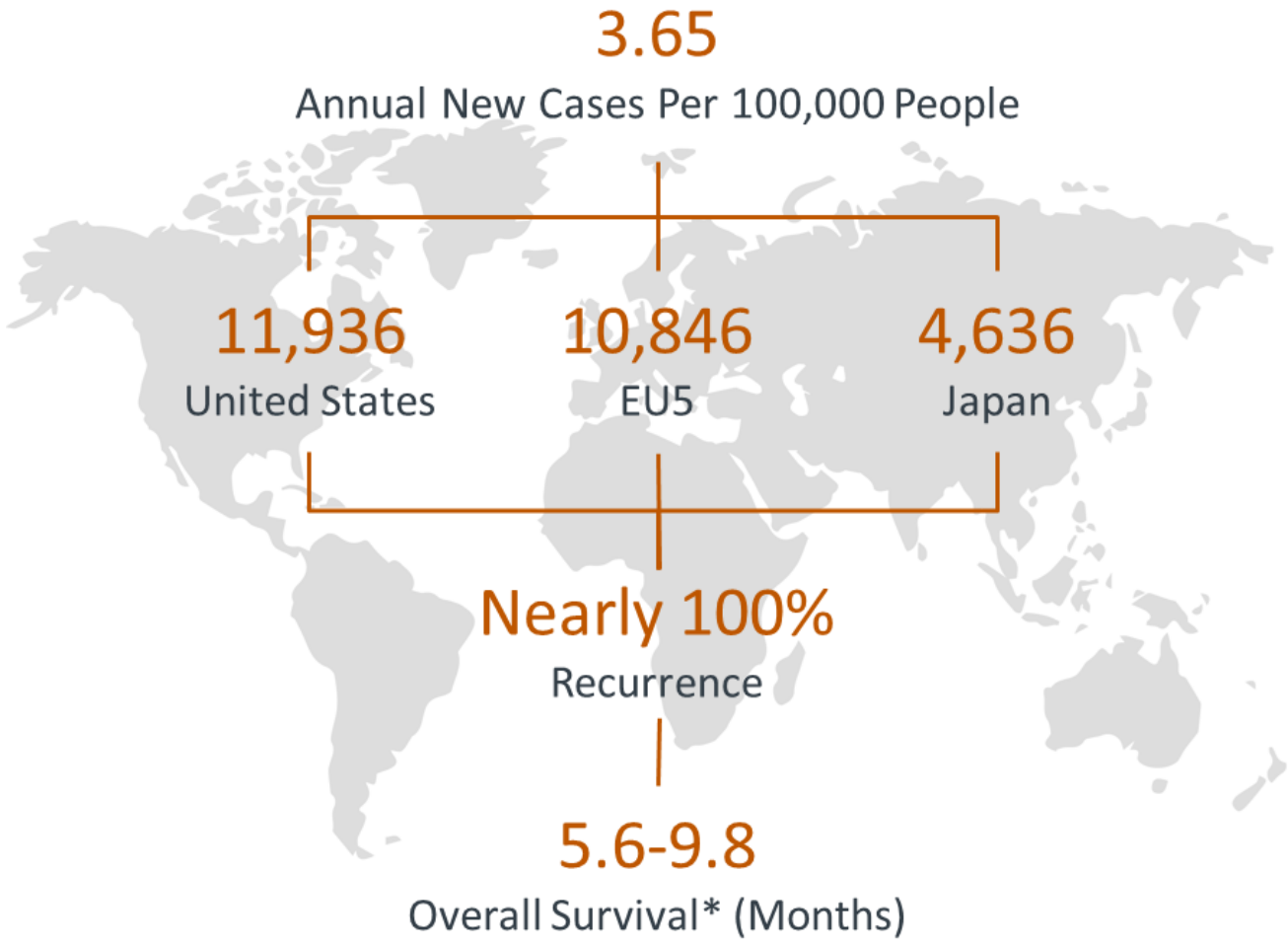
* proprietary, innovative ** complex generic

Rhenium-186 NanoLiposome (RNL™) for the Treatment of Recurrent Glioblastoma

Gregory Stein, M.D., M.B.A.
Senior Vice President, Clinical Development of
Plus Therapeutics

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Recurrent Glioblastoma: A Death Sentence

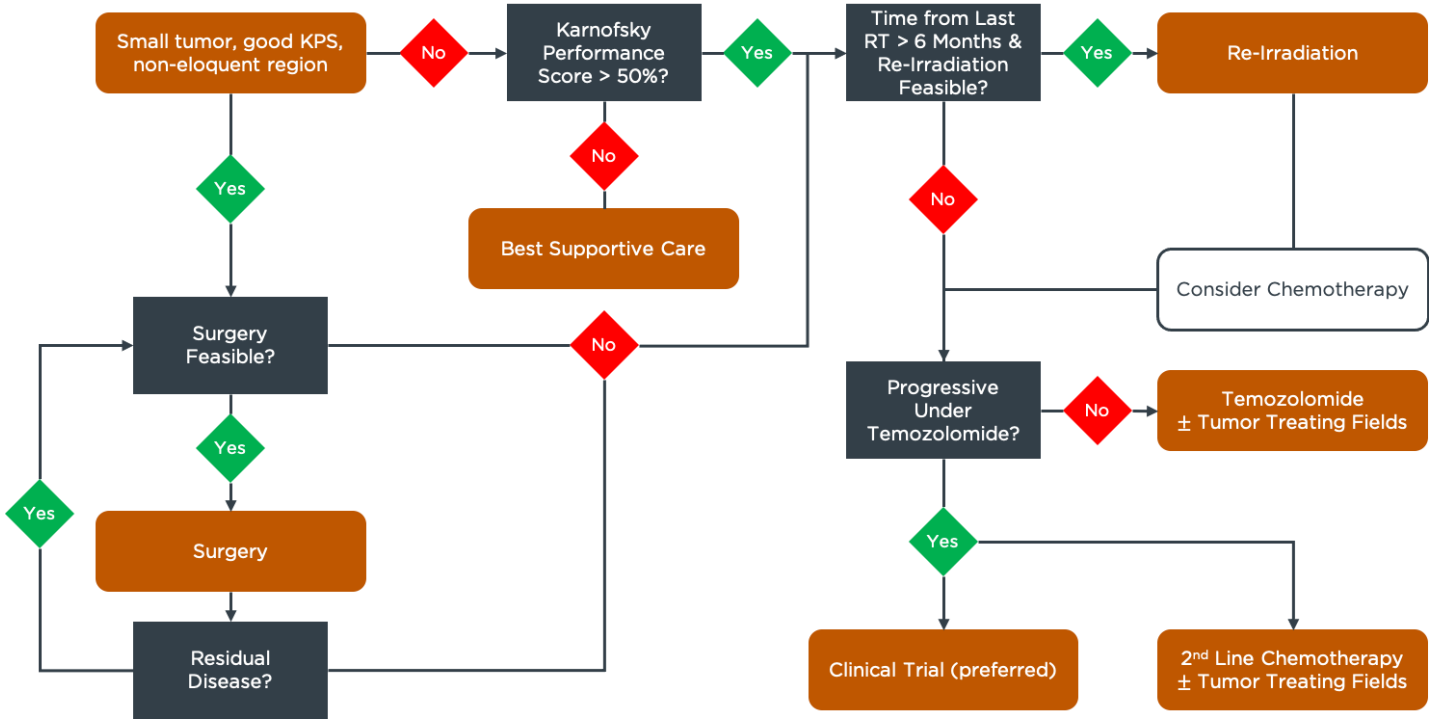


Sources: CBTRUS; Glas M. *Ther Adv Med Oncol* 2019

*From time of firstrecurrence

Recurrent Glioblastoma Treatment: No Consensus or Compelling Options

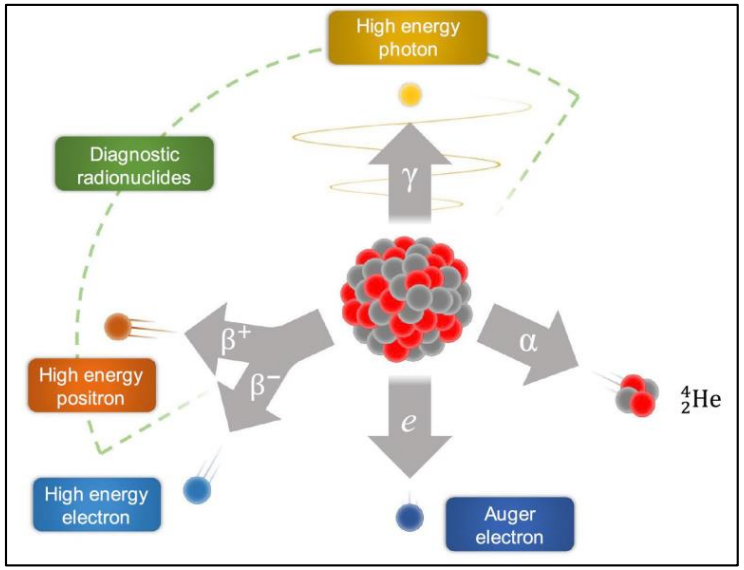
- Standards of care in tumor recurrence are less well-defined than for primary tumors
- Options include second surgery, re-irradiation, additional temozolomide, bevacizumab, and other drugs
- All options are palliative and provide very limited benefit
- Patients and providers are seeking new treatment options for recurrent glioblastoma with improved safety and efficacy

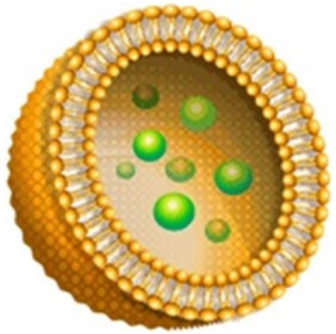


*From time of firstrecurrence

Therapeutic Construct: Rhenium-186 NanoLiposome (RNL)

Rhenium-186	+Beta and Gamma energy emitter +2-4 mm Range & 90-hour half-life
BMEDA Chelator	+Required to form stable nanoliposome with Rhenium-186
NanoLiposome	+Liposome construct of ~100 nm diameter
Convection Enhanced Delivery (CED)	+Most effective method of local tumor delivery using hydrostatic pressure to distribute RNL



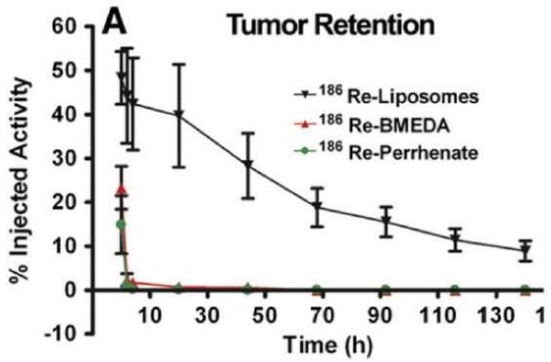


RNL™

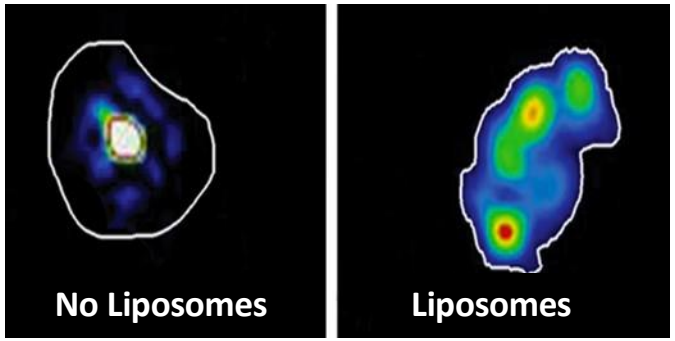
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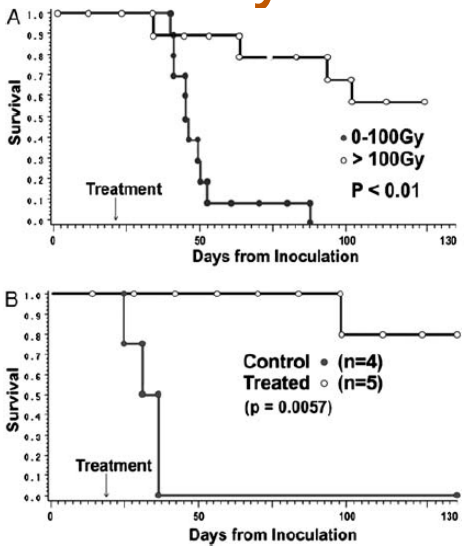
RNL Preclinical Science: Retention, Tumor Coverage, Efficacy, and Safety

Liposomal encapsulation fundamentally changes both the **retention** within the tumor and the **dispersion** of the drug product.

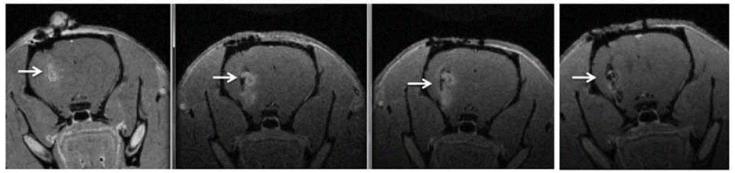


Tumor Dispersion

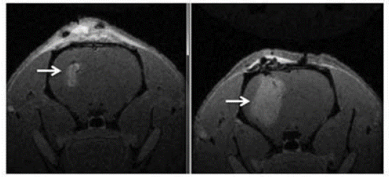




^{186}Re-Liposome Treatment



Control





+ Intracranial administration of 1, 3.5 or 6 mCi RNL produced no significant pathologic changes at 24 hours or 14 days

+ Highest absorbed dose was 360 Gy

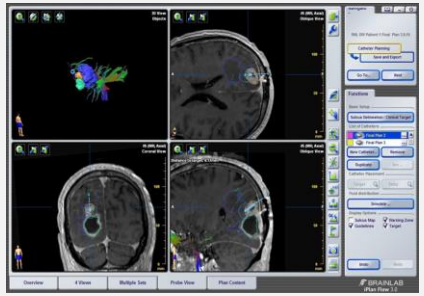
+ Based on these data, the no adverse effect limit (NOAEL), as related to brain pathology, was determined to be an absorbed dose of 360 Gy

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

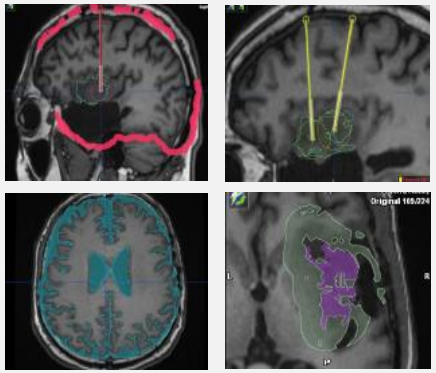
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ReSPECT Therapeutic Planning & Treatment

PreOP Treatment Planning	Day 1 Operating Room	Day 2 RNL Infusion	Day 3 – 4 Discharge Home



Tumor Targeting & Coordinates



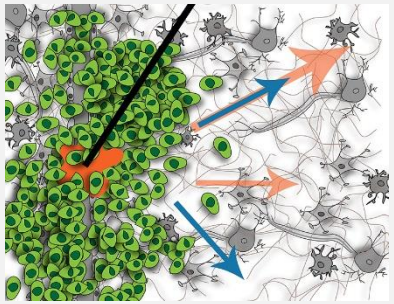
Optimal Catheter Trajectory



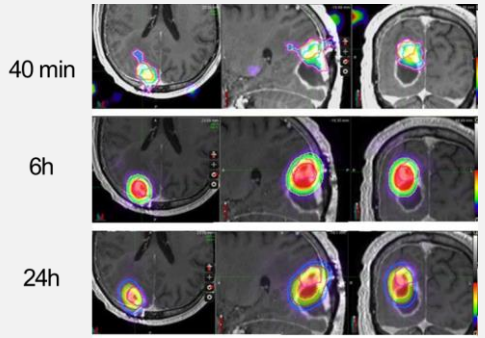
Planning Data Input to OR Computer



Stereotactic Catheter Placement



Convection Enhanced Delivery



Real Time Imaging of RNL Therapy



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ReSPECT Phase 1 Trial – Interim Data

Andrew J. Brenner, M.D., Ph.D.
Associate Professor of Medicine, Neurology, and Neurosurgery
The University of Texas, Health Services Center at San Antonio

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ReSPECT U.S. Phase 1 Clinical Trial

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

- Study design: Single arm, prospective 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 I dose escalation trial and a subsequent cohort at the recommended phase 2 dose).
- 5th dose escalation cohort complete
- First patient in 6th cohort recently treated
- 16 patients treated thus far with RNL

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 Dose Escalation Status

Cohort	Infused Volume (mL)	Total RNL Activity (mCi)	Concentration (mCi/mL)	Status
1	0.66	1.0	1.5	First 5 cohorts completed (n = 15 patients)
2	1.32	2.0	1.5	
3	2.64	4.0	1.5	
4	5.28	8.0	1.5	
5	5.28	13.4	2.5	
6	**8.80**	**22.3**	**2.5**	**1 pt treated to-date**

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ReSPECT Phase 1 Data Summary (n = 15)

Patient	Dose (mCi)	Volume of Infusate [Vi] (mL)	Conc. (mCi/mL)	Catheters	Maximum Flow Rate (µL/min)	Prior Treatment Cycles	Beva-cizumab Failure	Overall Survival (months)	Alive*
1	1.0	0.66	1.5	1	5	1	N	30.0	N
2	1.0	0.66	1.5	1	5	1	N	33.0	N
3	1.0	0.66	1.5	1	5	2	N	8.6	N
4	2.0	1.32	1.5	1	5	3	Y	1.6	N
5	2.0	1.32	1.5	1	5	1	N	10.8	N
6	2.0	1.32	1.5	1	5	2	Y	5.7	N
7	4.0	2.64	1.5	1	5	2	Y	4.1	N
8	4.0	2.64	1.5	1	5	2	Y	5.7	N
9	4.0	2.64	1.5	1	5	2	Y	4.1	N
10	8.0	5.28	1.5	1	10	3	Y	4.8	N
11	8.0	5.28	1.5	2	10	2	Y	4.9	N
12	8.0	5.28	1.5	2	10	1	N	22.4	Y
13	13.4	5.28	2.5	2	10	3	N	11.5	Y
14	13.4	5.28	2.5	3	15	2	N	4.0	Y
15	13.4	5.28	2.5	3	15	2	N	3.8	Y

*As of 10/30/2020

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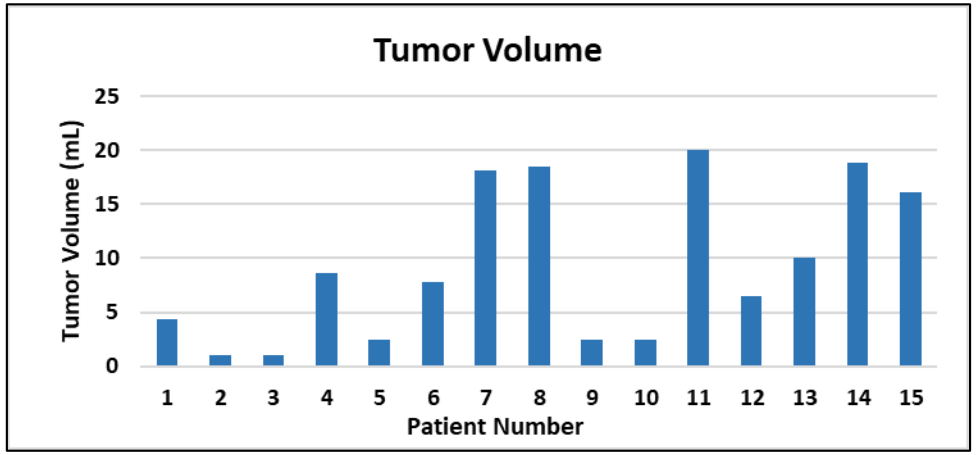
ReSPECT Phase 1 Safety Data

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

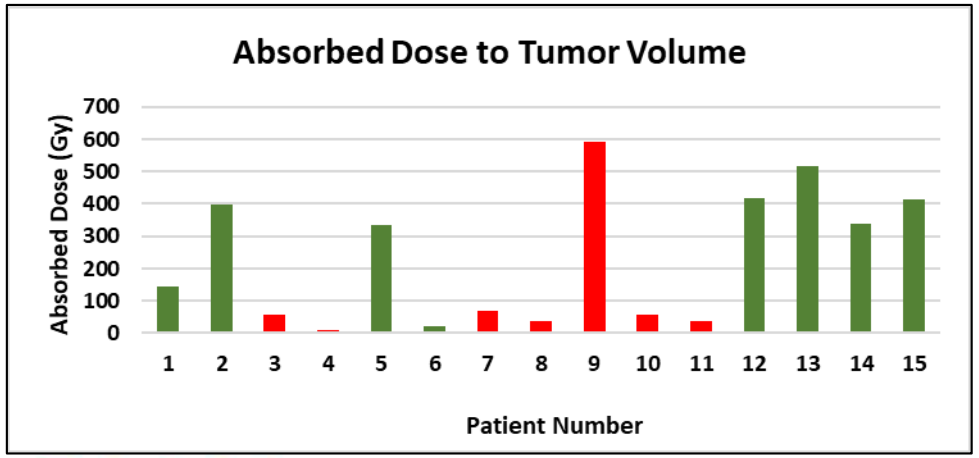
- The Adverse Events (AEs) with the highest incidence were: Fatigue (40%), Diarrhea (27%), Gait Abnormality (27%), Headache (27%), Hemiparesis (27%), Lightheadedness (20%), Scalp Discomfort (20%), Seizure (20%) and Cerebral Edema (20%).
- Neither the incidence nor severity of AEs appeared to increase with increasing doses of RNL.
- Four Serious Adverse Events (SAEs) were reported: Seizure in 3 patients and Cerebral Edema in 1 patient. However, none of the SAEs was considered causally related to RNL.
- Most AEs were considered causally unrelated to RNL except scalp discomfort, which was considered related to the surgical procedure.

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Tumor Volumes and Absorbed Doses



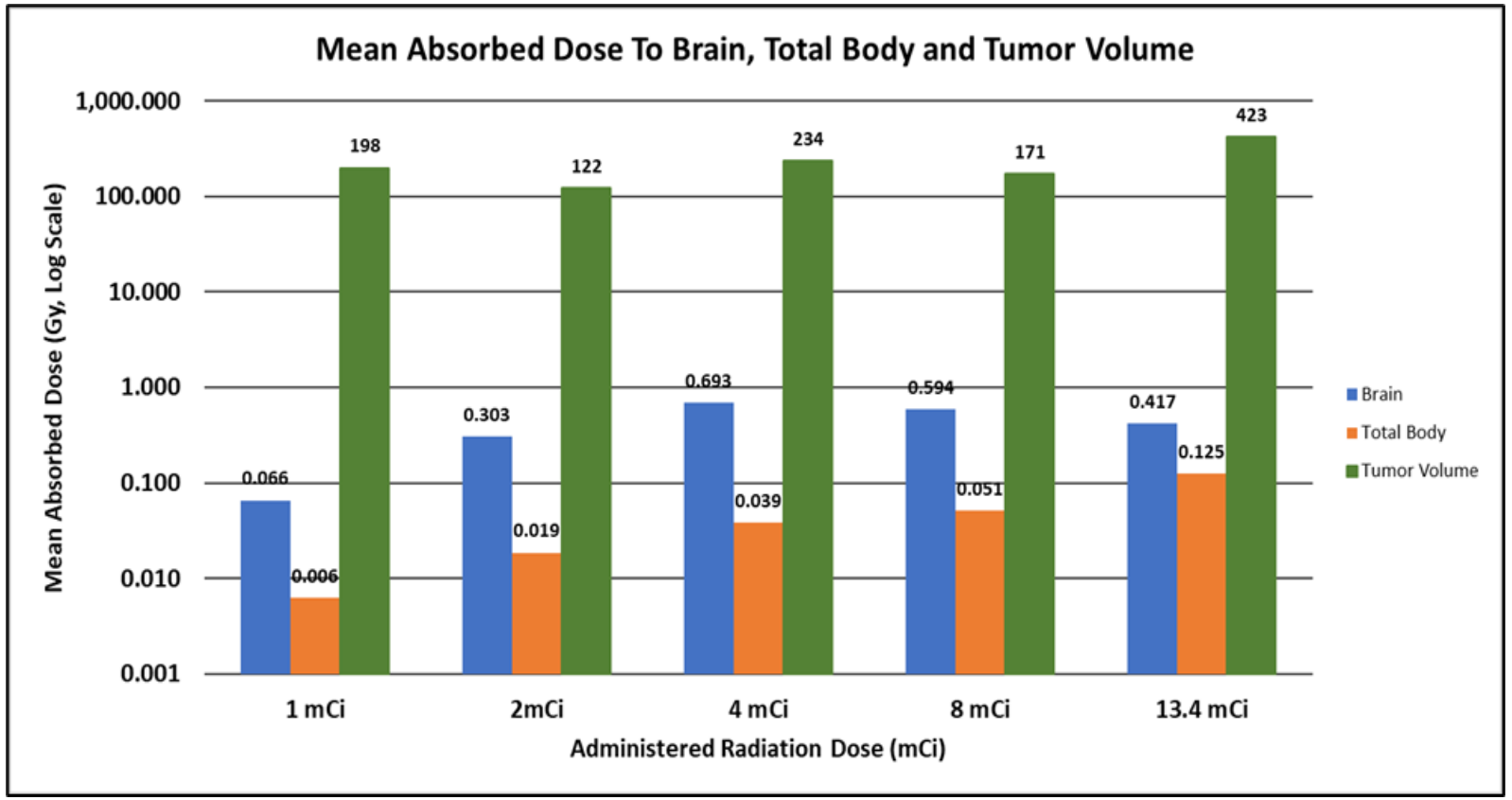
- Mean and median tumor volumes are 9.2 and 7.8 mL, respectively
- Tumor volume range is 1.1 mL to 20.0 mL



- Median absorbed dose (AD) to the tumor volume across all subjects (n=15) was 143 Gy (range 9 – 593).
- Median AD in subjects who had failed bevacizumab (n=7) was 38 Gy (range 9 – 593).
- Median AD in subjects who were bevacizumab-naïve (n=8) was 367 Gy (range 56 – 517).
- The maximum absorbed dose to the tumor volume was 593 Gy.
- The mean retention of the administered dose at 24 hours was 64% (CI 50 – 78).
- Prior administration of bevacizumab (red) appears to negatively impact convection.

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ReSPECT Phase 1: High Absorbed Doses to Tumor Volume But Not to Brain or Total Body



- The total body absorbed dose ≤ 0.15 Gy.
- The mean absorbed dose to the organs ≤ 0.70 Gy.
- The ratio of the mean tumor volume absorbed dose to the mean total body absorbed dose in the last two cohorts ≥ 3,000.

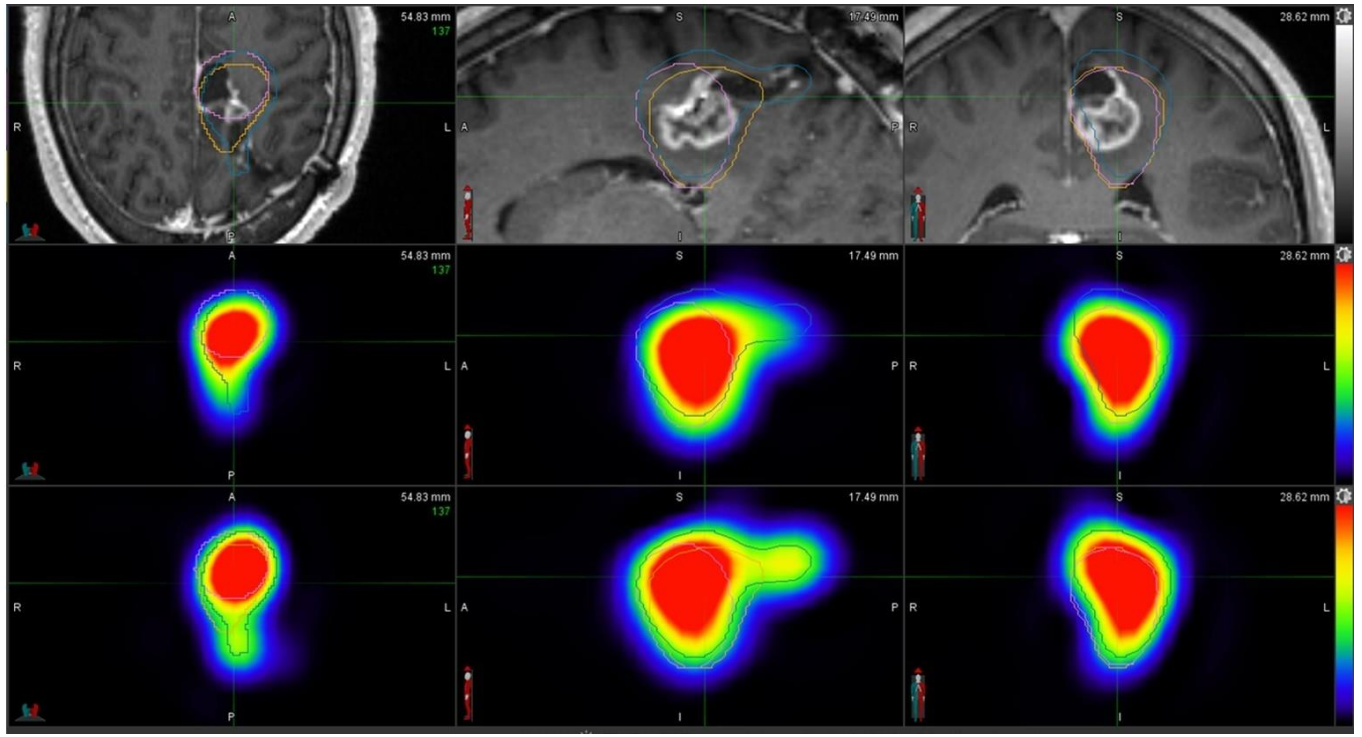
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Subject 01-014 Treatment Summary

MRI

SPECT
24 hr

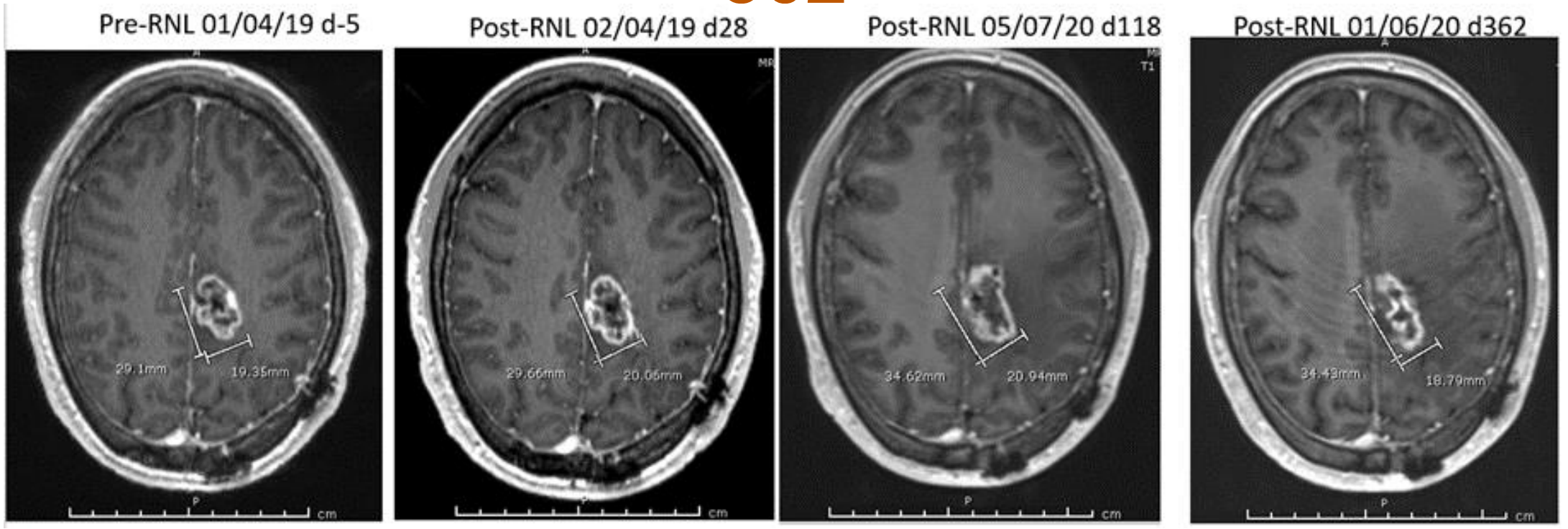
SPECT
120 hr



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

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Subject 01-014 Tumor Response Observed at 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)

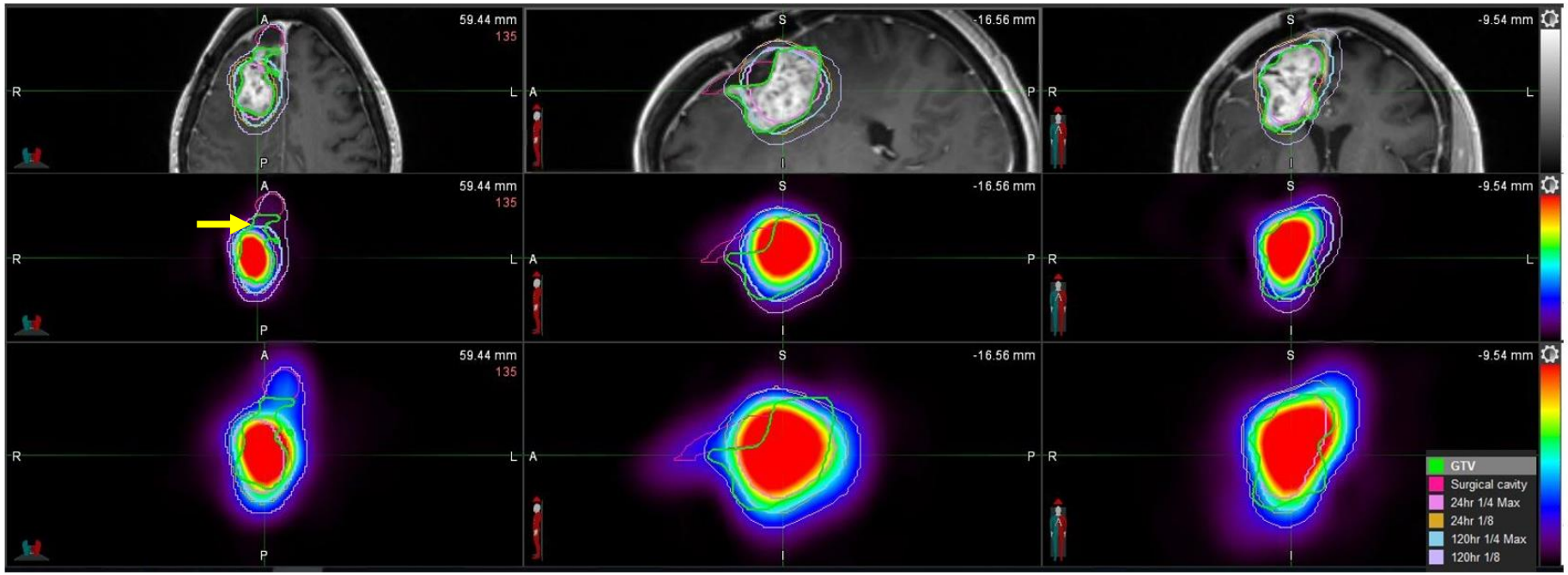
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Subject 01-017 Treatment Summary

MRI Baseline

SPECT 24 hr

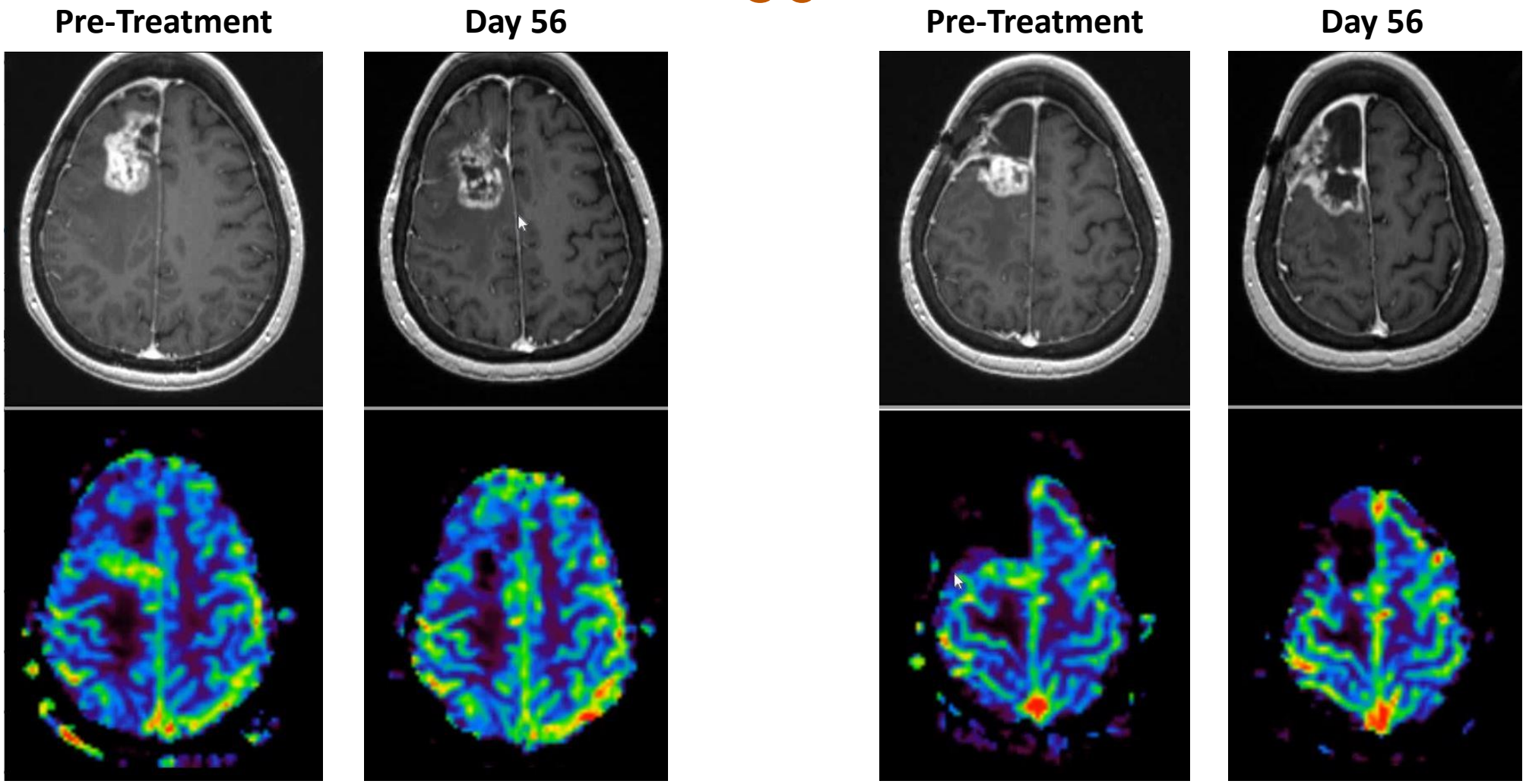
SPECT 120 hr



- Tumor volume was 18.8 mL and tumor coverage was 87%
- Absorbed dose delivered to tumor was 336 Gy
- At 24 hours, anterior portion of the tumor (yellow arrow) was outside Vd (gold line)
- By Day 5, the entire tumor was within the Vd (light purple line)

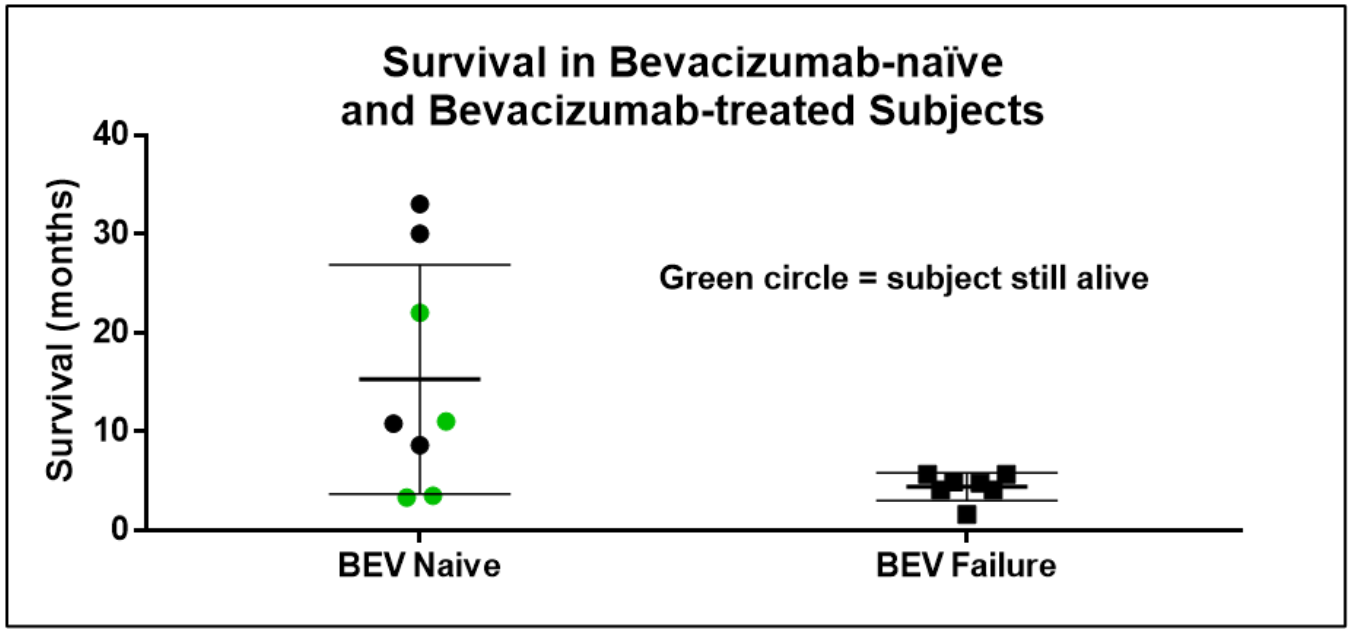
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MRI & Perfusion Imaging of Subject 01-017 at Post Op Day 56



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RNL: Survival Based on Prior Bevacizumab Use



- Median survival duration in subjects that had failed bevacizumab (n=7) was 4.8 months.
- Median and mean survival duration in subjects that were bevacizumab-naïve (n=8) is currently 11.0 months (range 3.5 – 33) and 15.4 months (95% CI 7.4 – 23.4), respectively, with 4 patients still alive.

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ReSPECT Phase 1 Trial Conclusions

- Intratumoral RNL can deliver up to **15 times** the absorbed dose of radiation administered by EBRT **without significant toxicity**.
- These data indicate that intratumoral administration of RNL by CED at doses up to 13.4 mCi in 5.28 mL of infusate is safe and well-tolerated.
- No treatment related adverse events noted thus far and maximum tolerated dose not yet reached.
- Prior administration of bevacizumab appears to negatively impact convection of RNL.
- Current status: cohort 6 with a RNL dose of 22.3 mCi and infusate volume 8.8 mL has begun.

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Patient Experience and Perspective

Phyllis M.

ReSPECT Clinical Trial Patient

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Closing Remarks

Marc Hedrick, M.D.
President and Chief Executive Officer
Plus Therapeutics

Forthcoming Milestones for 2020 & 2021

+ Complete enrollment in U.S. ReSPECT Phase 1 clinical trial
+ Report final ReSPECT data & Phase 2/pivotal dose recommendation
+ Potentially seek U.S. FDA Breakthrough Therapy Designation for RNL in rGBM
+ Potentially seek EMA Orphan Drug Designation for RNL in rGBM
+ Complete key CMC and GMP commercial scale-up activities for RNL
+ Optimize regulatory strategy & follow-on clinical trial plan for RNL in rGBM
+ Complete IND-enabling studies for 1st follow-on RNL indication
+ Seek CPRIT support for ongoing RNL development
+ Seek partner support for RNL™, DocePLUS™ & DoxoPLUS™ assets

Q&A

Marc Hedrick, M.D.
President and Chief Executive Officer, Plus Therapeutics

Gregory Stein, M.D., M.B.A.
Senior Vice President, Clinical Development, Plus Therapeutics

Andrew J. Brenner, M.D., Ph.D.
Associate Professor of Medicine, Neurology, and Neurosurgery
The University of Texas, Health Services Center at San Antonio

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Thank you

If you have any questions please contact us at

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