PLUS Corporate Presentation

July 2020

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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Our mission is to become the world's leader in developing better and safer nanoscale oncology drugs to improve survival and quality of life for both pediatric and adult patients.

PLUS

Investment Highlights

- Proprietary nanoparticle drug development platform
  - Three clinical stage drugs
  - Lead drug trial funded by NIH/NCI
  - Multiple opportunities in preclinical development
- Capital efficient drug development model
  - Small core team & low fixed overhead costs
  - New Texas HQ opens up $6B in State of Texas oncology-focused CPRIT funding
  - 12-18 months cash
- Key 2020 milestones
  - Clinical data in brain cancer therapy
  - Deal pipeline
  - New drug pipeline clinical candidates

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Drug Development Pipeline

RNL™

Proprietary Innovative BMEDA-Chelated Rhenium NanoLiposome

DocePLUS™

Proprietary Innovative Albumin-Stabilized PEGylated Liposomal Docetaxel

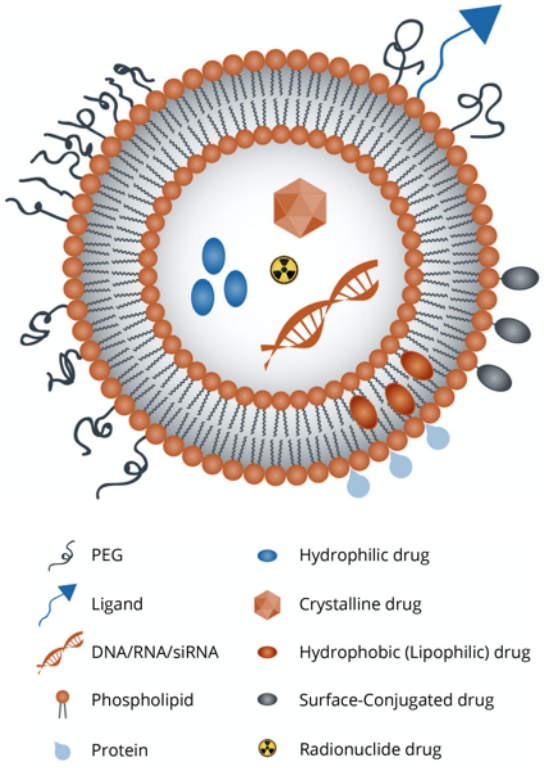
DoxoPLUS™

Generic PEGylated Liposomal Doxorubicin

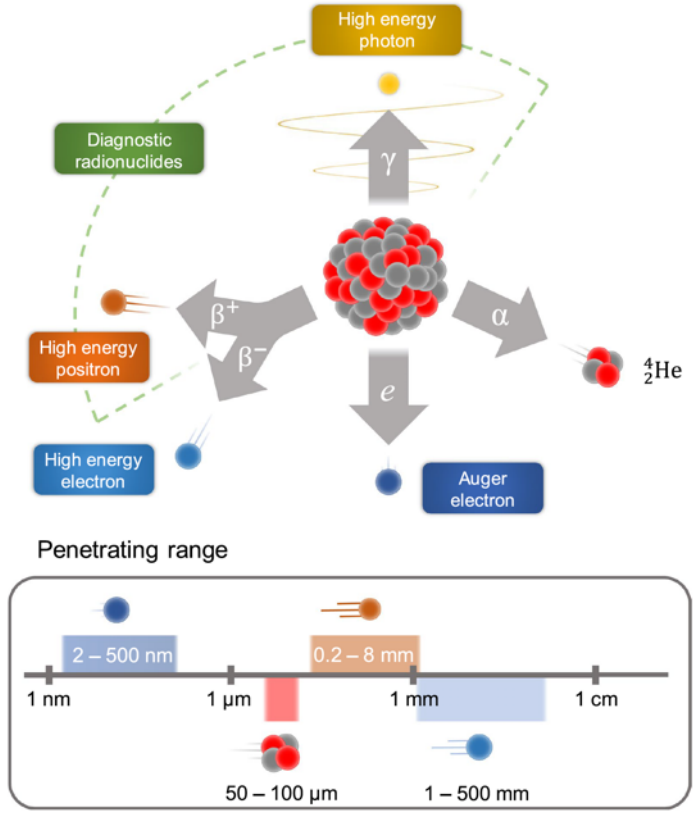
PROGRAM	INDICATION	DELIVERY	DESIGNATION	FUNDING	PRECLINICAL	CLINICAL
RNL™	Recurrent Glioblastoma	Intratumoral	-	NIH/NCI	Complete	Phase 1 Enrolling
RNL™	Multiple	Intratumoral/ Intravenous	-	-	Data published/ further studies in progress	
DocePLUS™	Small Cell Lung Cancer	Intravenous	FDA Orphan Drug	-	Complete	Phase 1 Complete
DoxoPLUS™	Breast/Ovarian Cancer	Intravenous	-	-	Complete	Bioequivalence Complete

Technology Platform

Nanoparticle Design & Manufacturing



Radionucleotide Encapsulation & Delivery



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Recent Transaction

PLUS Licenses Novel Brain Cancer Therapy

Rationale

+ Create long-term value through a substantially expanded and strengthened new clinical & preclinical drug pipeline

Key Terms

+ Plus provides $400K in cash & $300K in common stock
+ Plus obligated to development and sales milestone payments of up to $136.5M
+ Plus pays a single-digit royalty on US and European sales

Andrew Brenner, MD PhD
Neuro Oncology

William Phillips, MD
Nuclear Medicine

Ande Bao, PhD
Radiation Physics

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NIH
National Institutes of Health

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

CPRIT

UT Southwestern Medical Center

Radiotherapeutics: Deal & Pricing Economics

Recent FDA Approvals

Radiotherapy	Description	Indication	U.S. Launch	Annual Cost
Progenics AZEDRA®	iobenguane I-131	pheochromocytoma or paraganglioma (ultra rare)	2018	$294K
Novartis LUTATHERA®	lutetium Lu-177	gastroenteropancreatic neuroendocrine tumor (rare)	2018	$190K
Bayer XOFIGO®	radium Ra-223	prostate cancer	2013	$69K
Acrotech ZEVALIN®	Rituxan + yttrium Y-90	follicular B-cell Non-Hodgkin's lymphoma	2002	$28K

Recent Deals

- **2019:** Fusion Pharma raises $105M to support development of targeted radiotherapeutics for cancer
- **2018:** Novartis acquires Endocyte for $2.1B, gaining drug conjugation technology to develop targeted therapies with companion imaging agents including 177Lu-PSMA-617 for prostate cancer
- **2018:** Novartis acquires Advanced Accelerator Applications for $3.9B, gaining access to LUTATHERA® (lutetium Lu 177 dotatate) for neuroendocrine tumors; LUTATHERA® achieved global sales of $120M in the U.S. and Europe with an ongoing launch in Europe
- **2013:** Bayer acquires Algeta for $2.9B, gaining access to XOFIGO® (radium Ra 223 dichloride) for prostate cancer; XOFIGO® achieves global sales of $414M in 2018

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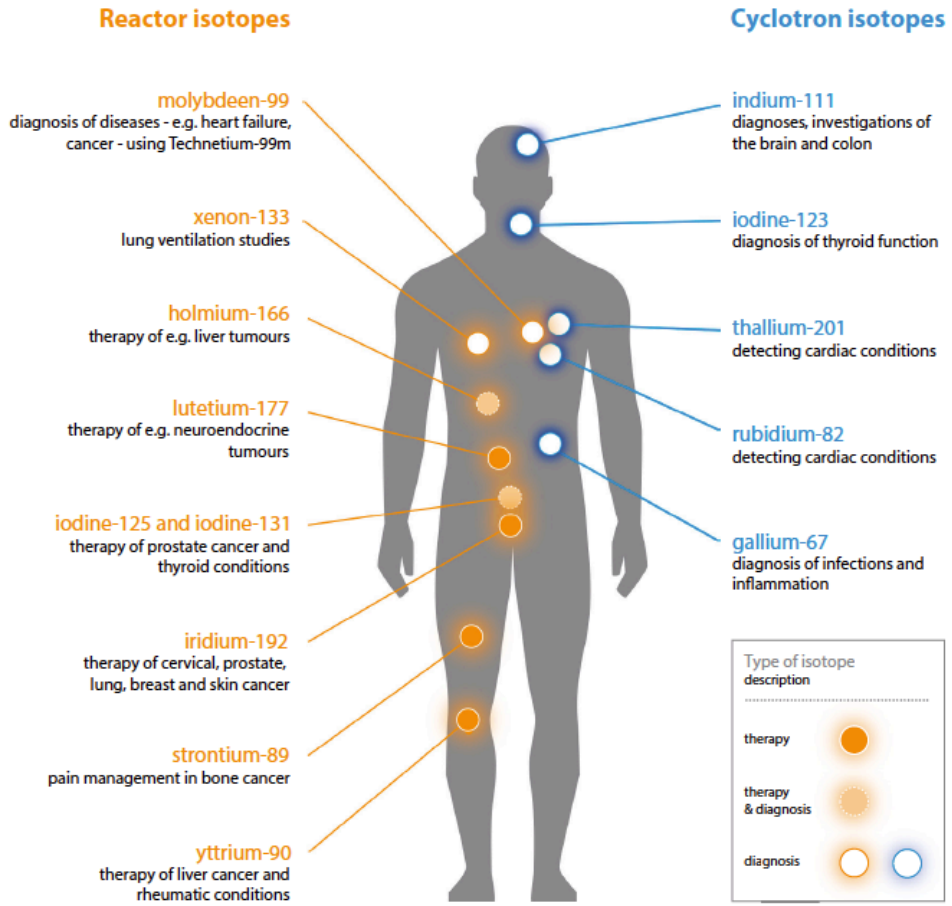
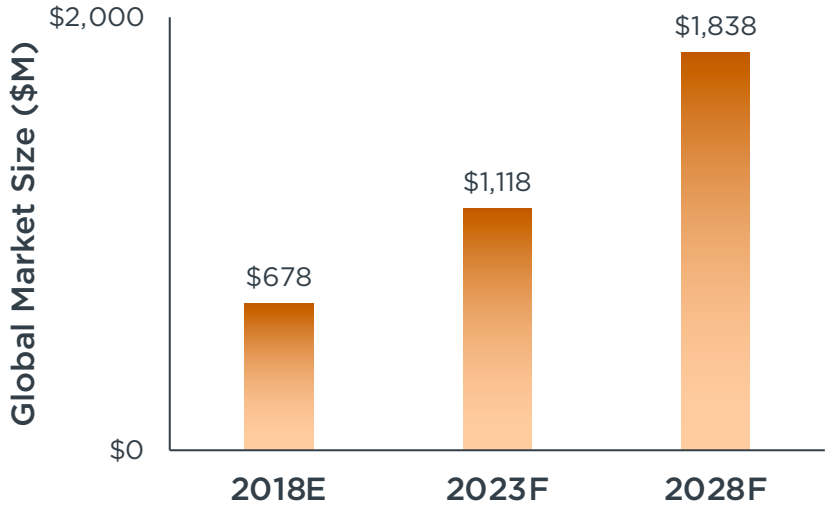
Sources: company websites, FiercePharma, LiveScience, Reuters, WSJ

Medical Radionuclide Market

Broad Diagnostic/Therapeutic Applications



Radiotherapeutics: Double-Digit Growth



- Produced in nuclear reactor
- Dual particle emitter: therapeutic & imaging
- Approved in Europe for the treatment of bone metastases
- Seamless integration in current hospital nuclear medicine workflows

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Sources: Nuclear Netherlands; Future Market Insights December 2018

Glioblastoma: A Death Sentence

Overall Survival

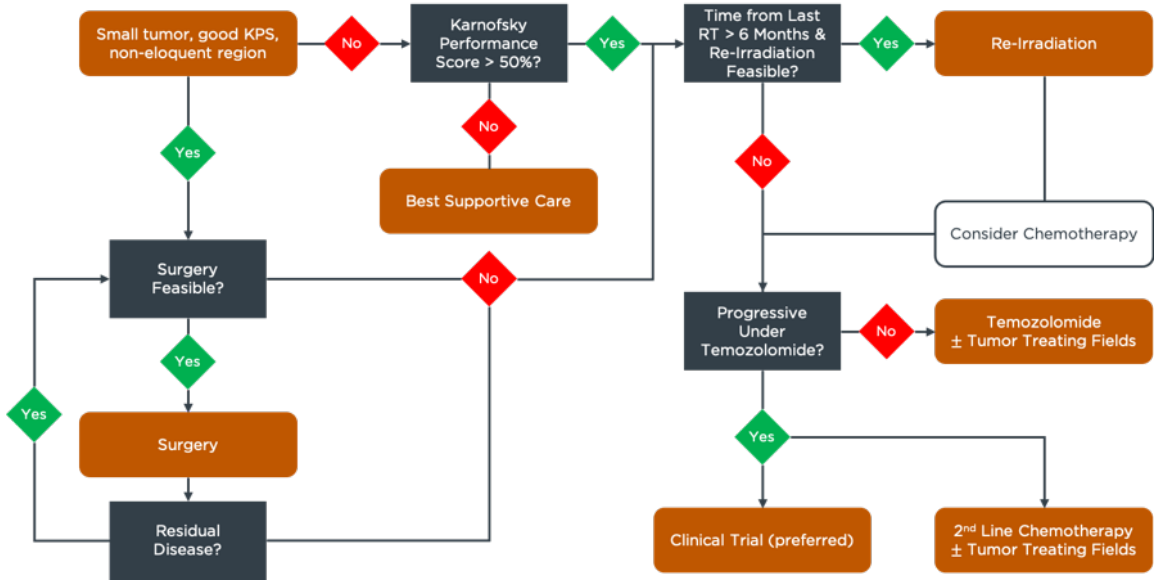
3.65
Annual New Cases Per 100,000 People

11,936	10,846	4,636
United States	EU5	Japan

Nearly 100%
Recurrence

5.6-9.8
Overall Survival* (Months)

Treatment Algorithm for Recurrent Cancer



- Tumor recurrence after primary therapy is the norm
- Standard of care in recurrent setting is ill-defined
- Only 1 new therapy FDA approved since 2011
- Patients and providers are seeking new treatment options

*From time of first recurrence

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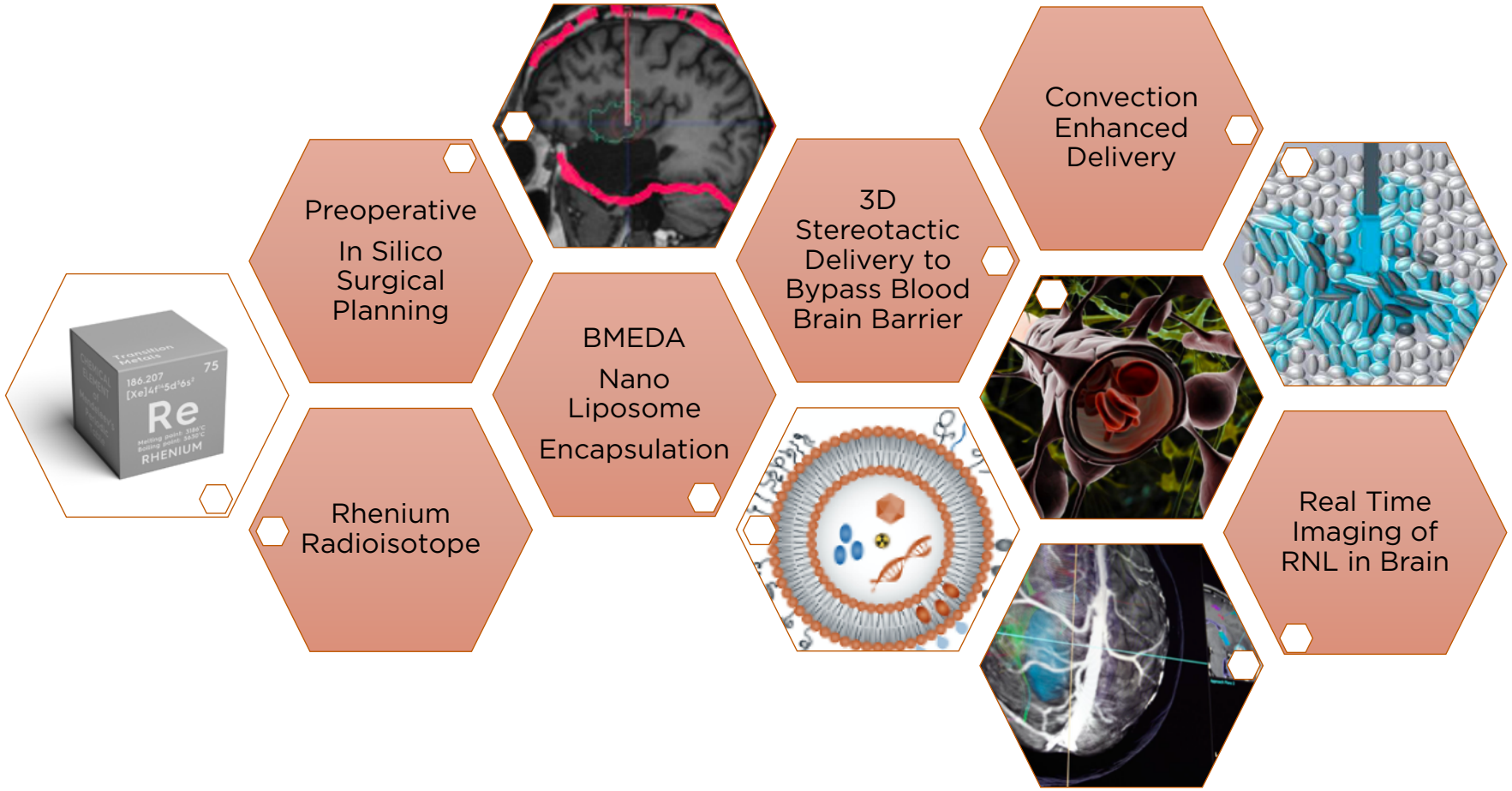
Sources: CBTRUS; Glas M. *Ther Adv Med Oncol* 2019

Solving the Therapeutic Puzzle for Brain Cancer

Multimodal Therapy with Rhenium NanoLiposome (RNL™)



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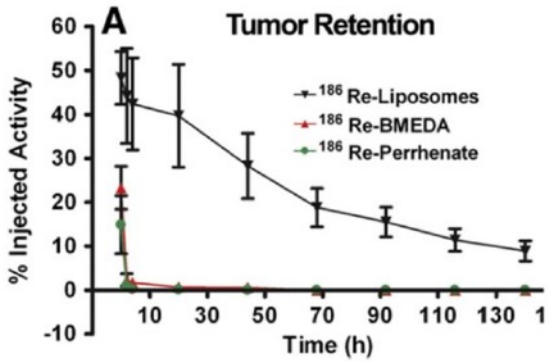
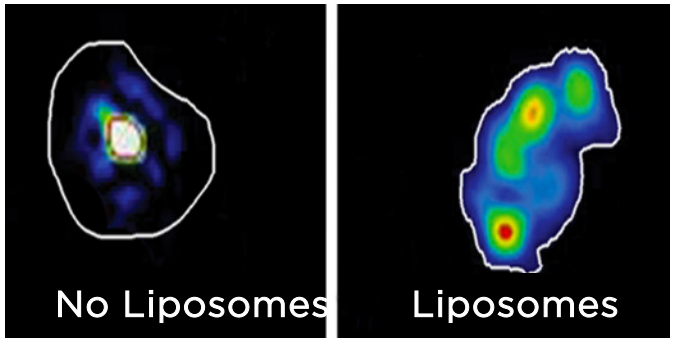
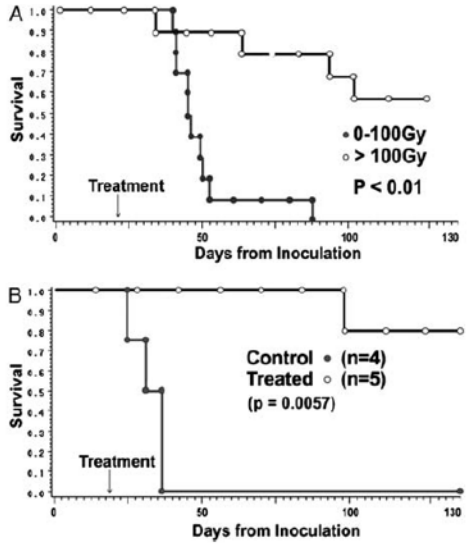
RNL™ Preclinical Science: Retention, Tumor Coverage & Safety

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

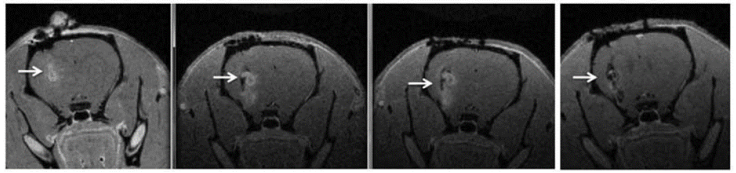


Tumor Dispersion

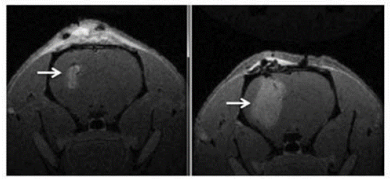


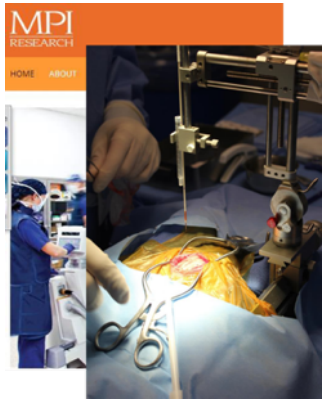


^{186}Re-Liposome Treatment



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

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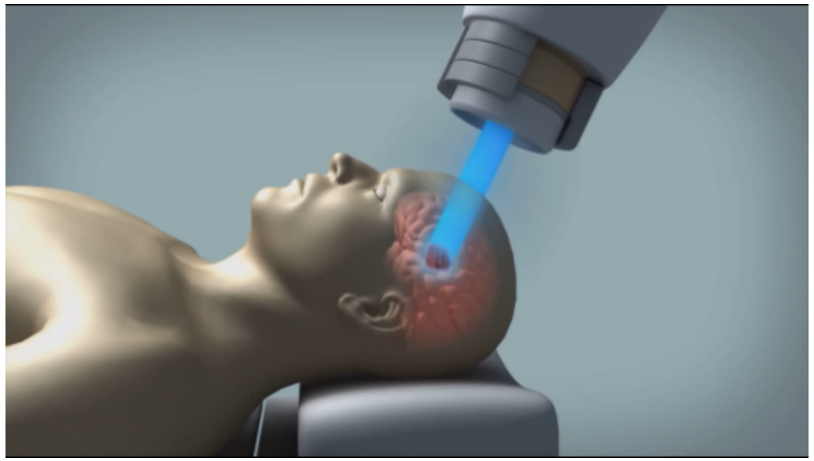
Source: Phillips, W. et al Advanced Drug Delivery Reviews 2014

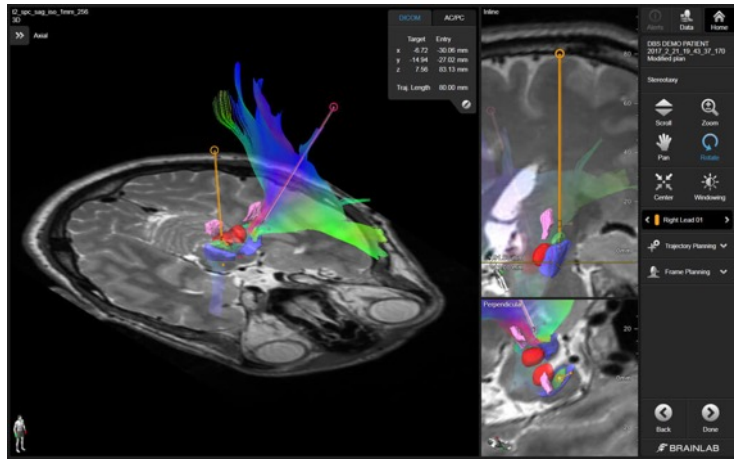
External Beam Radiation Therapy vs. RNL™

External Beam Radiation



- Significant radiation exposure to external tissues
- Safe dosing limited to 80/40 Gy
- Limited to ‘enhancing’ tumors
- Delivered over 4 weeks, 5x per week

RNL™ Radio Nanoliposome



- No exposure to external tissues
- Maximum safe dose not reached, >500Gy
- Micro fields cover non enhancing tumor
- ‘One-shot’ treatment via convection enhanced delivery

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RNL™: Enrolling Phase 1 Clinical Trial (NCT01906385)

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

- 5th dose escalation cohort complete and 15 patients treated thus far with RNL™
- Estimated treatment volume in 6th cohort will accommodate tumors up to 4.5cm
- Thus far, two patients survived > 30 months (vs. median survival of 9 months with best available care)
- For patients with RNL tumor coverage >75% (n=6):
  - average absorbed dose was 400 Gy (> 10X typical EBRT dose in re-irradiation of rGBM)
  - average survival thus far is 17.2 months (range 4.1 – 33.0)
- No treatment-related SAEs observed
- Early signals of efficacy in patients with adequate dosing and tumor coverage
- Supported by a $3M NIH/NCI grant through Phase 2

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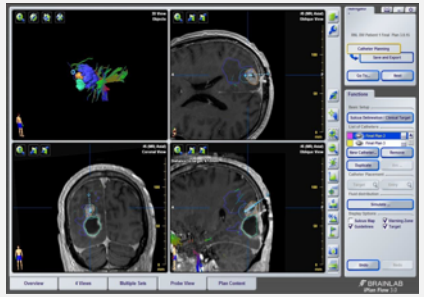
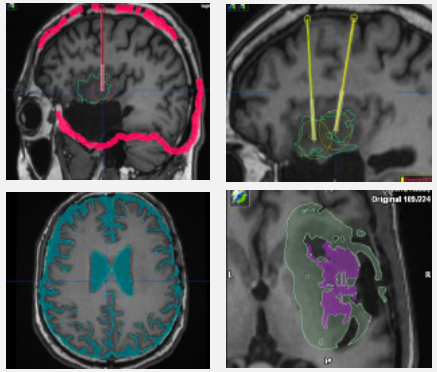
Therapeutic Planning & Treatment

PreOp
- *In Silico* Treatment Planning



Tumor Targeting & Coordinates



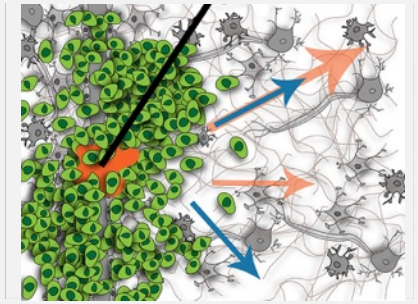
Optimal Catheter Trajectory

Day 1
- Operating Room

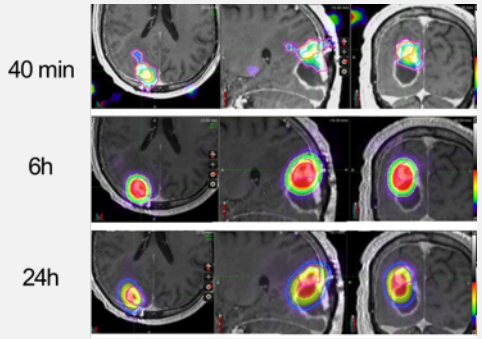
Planning Data Input to OR Computer

Stereotactic Catheter Placement

Day 2
- RNL™ Infusion



Convection Enhanced Delivery



Real Time Imaging of RNL™ Therapy

Day 3/4
- Patient Discharge

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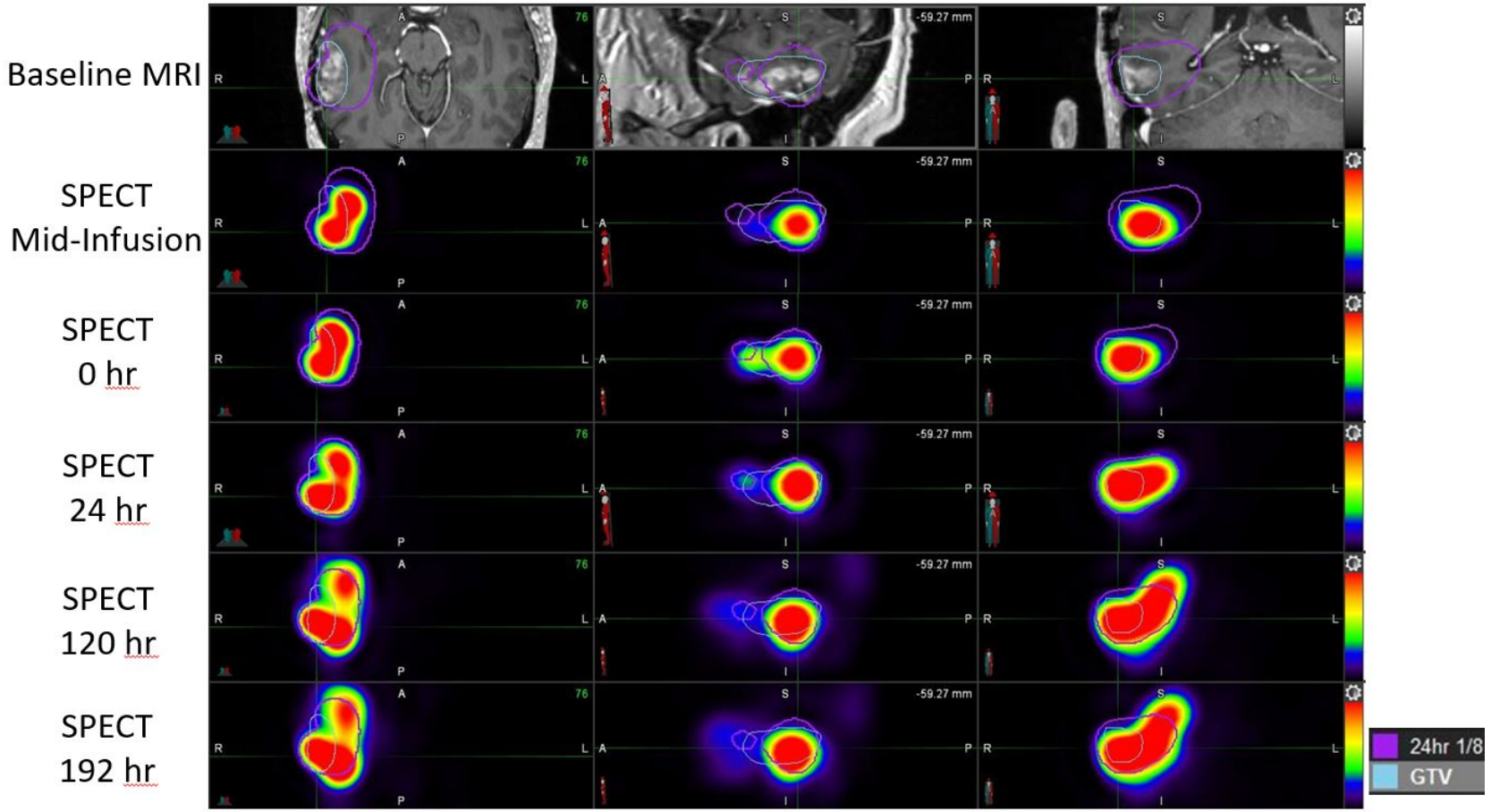
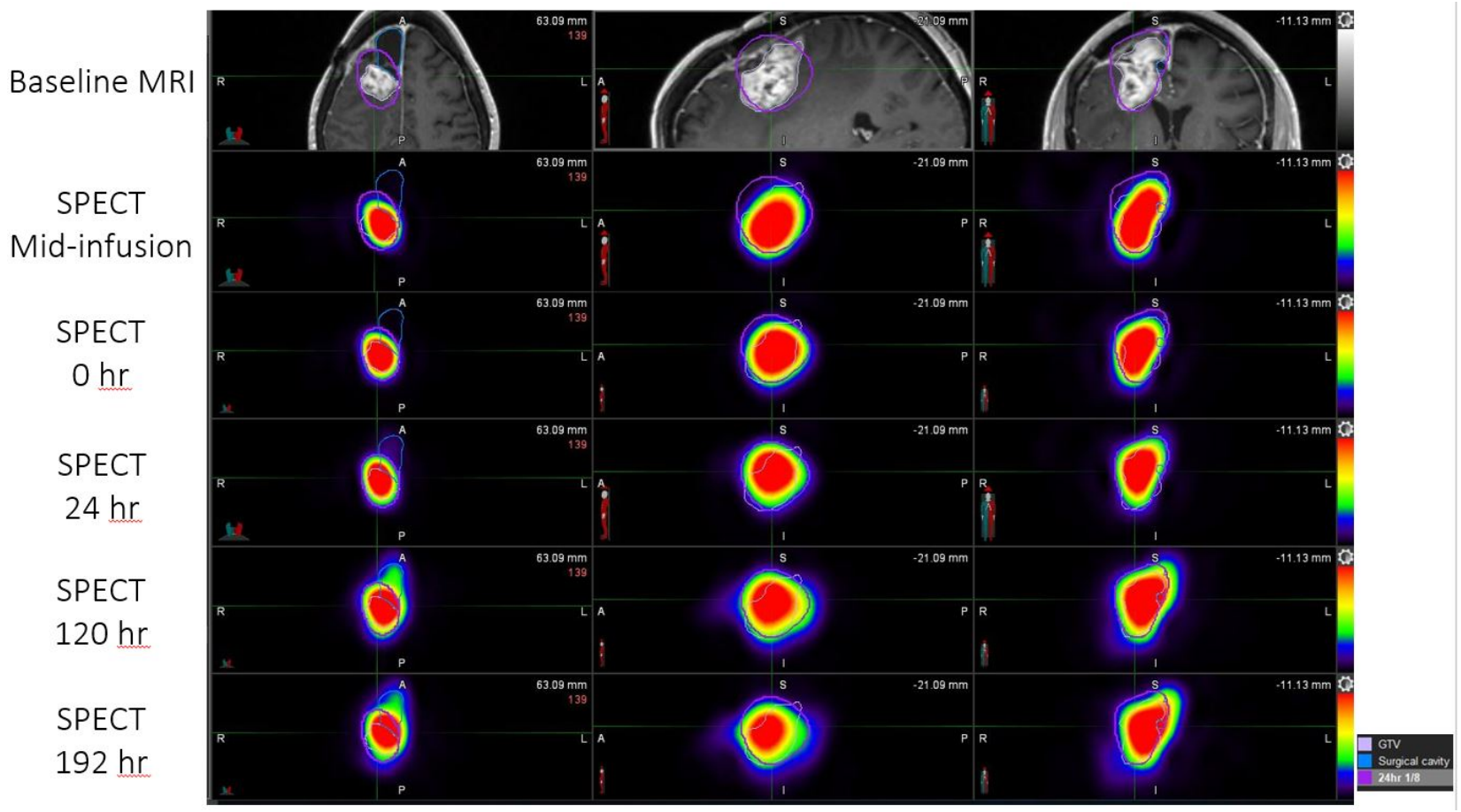
Sequential Imaging of Cohort 5 Patient 13

Serial SPECT scans demonstrate excellent tumor coverage and retention out to Day 8

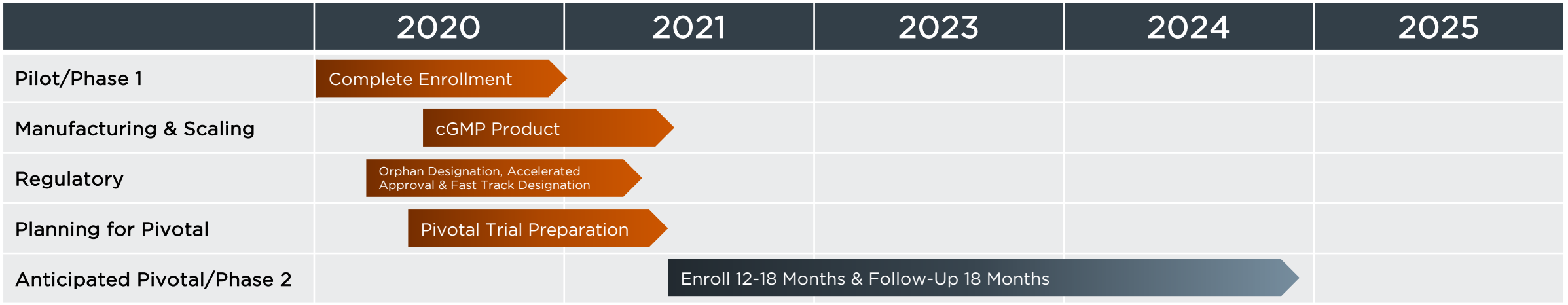


Sequential Imaging of Cohort 5 Patient 14

Serial SPECT scans demonstrate excellent tumor coverage and retention out to Day 8



RNL™ Development Plan



- Phase 1 trial planned completion enrollment late 2020 (assuming minimal COVID-19 impact)
- Manufacturing and product scalability in place by mid 2021
- Seek US and EU orphan drug designation in 2020
- Seek US FDA accelerated & FastTrack designations in 2020
- Preparations for Phase 2 pivotal trial
- Initiate pivotal adaptive design Phase 2 clinical trial in H2 2021

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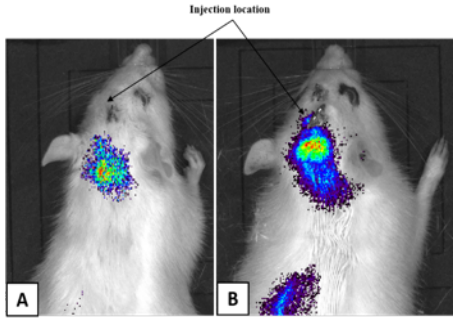
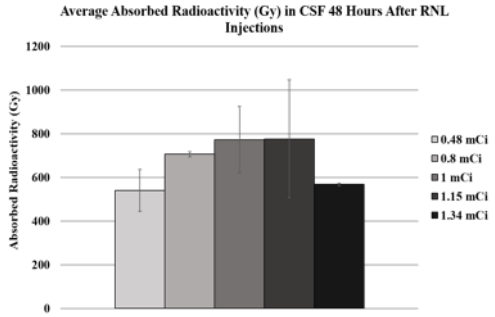
RNL™: Multiple Indication Expansion Opportunities

Leptomeningeal Carcinomatosis

62.5% of rodents injected with a single dose of RNL had a decrease in tumor size, suggesting that RNL may have therapeutic efficacy, after single administration

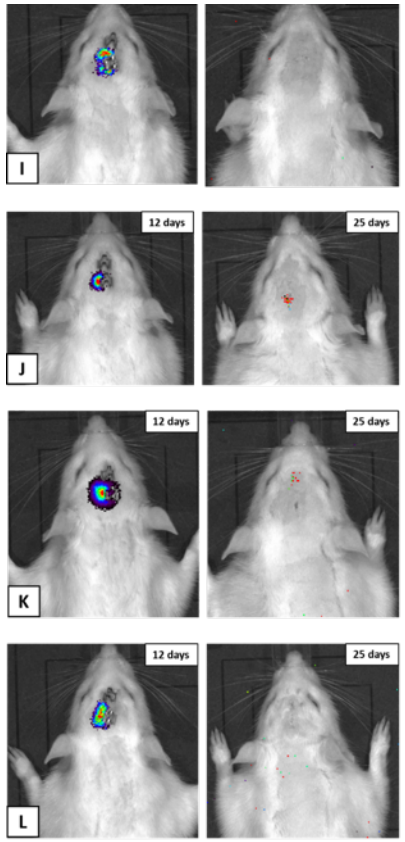


Leptomeningeal Model



Maximum Tolerated Dose

MTD not reached as all RNL cohorts gained weight, consumed enough foot to maintain energy and grow, and did not demonstrate any symptoms following dose administration. 1.34 mCi dose reported to be an outlier due to an unknown technical error.



Post treatment with RNL

PLUS

RNL™: Multiple Indication Expansion Opportunities

Peritoneal Carcinomatosis

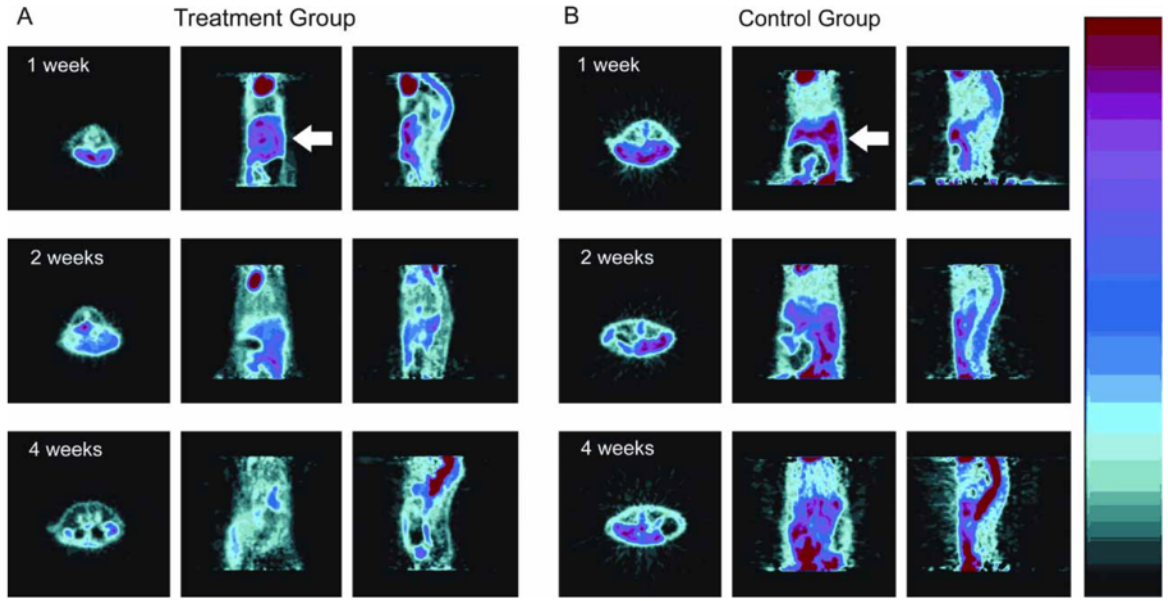


Figure 5. ^{18}F-FDG microPET images of the peritoneal cavity acquired 45 min post-injection at 1, 2, and 4 weeks post-treatment. (A) Corresponding transverse, coronal, and sagittal slices (left to right) of peritoneal cavity (arrow) in treatment group. The treatment group shows a gradual decrease in peritoneal ^{18}F-FDG activity over the 4 weeks post-treatment. (B) Corresponding transverse, coronal, and sagittal slices (left to right) of peritoneal cavity (arrow) in control group. The continued intense peritoneal uptake of ^{18}F-FDG in the control group over the 4-week period represents the accumulation of tumor cells in the peritoneal cavity. The color bar represents the intensity, where red is the maximum and black is the minimum. Please see online for color version.

Source: Zavaleta, C at al. J Drug Targeting 2008

20

DocePLUS™ is a Reformulation of Docetaxel

Key Features & Benefits

+ **Liposomal encapsulation**: creates an intravascular depot form of the otherwise highly lipophilic and insoluble docetaxel
+ **Albumin**: facilitates protein binding and minimizes the unbound fraction of docetaxel; stabilizes the liposome
+ **PolyEthylene Glycol (PEG)**: reduces capture of the liposome by the reticuloendothelial system and premature clearance from the circulation
+ **Convenience**: simple, 1-hour infusion once every 3 weeks
+ **Improved Pharmacokinetics**: 4- to 5-fold increase of total plasma docetaxel AUC compared with an equivalent dose of docetaxel using a standard vehicle
+ **Favorable Biodistribution**: preferentially accumulates into the liver and lung tissues

Value Proposition

+ Compared to IV docetaxel (TAXOTERE®), by encapsulating docetaxel in the lipid bilayer of a liposome and albumin, DocePLUS™ eliminates the need for Tween 80 and dexamethasone premedication that is used to reduce formulation-related hypersensitivity reactions
+ Based on the preclinical and clinical data, DocePLUS™ appears to be better tolerated than docetaxel and demonstrates improved efficacy with increasing doses without a concomitant increase in toxicity
+ Compared to NCEs, the approach with DocePLUS™ provides a lower relative development, clinical, regulatory, and commercial risk profile

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DocePLUS™ Phase 1 Study Key Findings

First-in-human, open-label, dose escalation (15-110 mg/m^2) study of DocePLUS™ in 29 heavily pretreated patients (~33% had prior TAXOTERE® exposure) with advanced solid tumors at 2 U.S. sites

Safety

+ DocePLUS™ achieved a 20% increase in MTD vs. standard docetaxel
+ 10 patients treated at MTD
    + Treatment-emergent adverse events included neutropenia, anemia, fatigue, and nausea
+ ~2-3 fold increase in AUC compared with free (non-encapsulated) docetaxel

Efficacy

+ 22 of 29 patients (76%) experienced stable disease
+ 1 patient with NSCLC and previous exposure to docetaxel had confirmed partial response to DocePLUS™
+ 2 prostate cancer patients had PSA reduction >95%: 1 patient was progression free for 54 weeks

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Cancer Chemother Pharmacol (2014) 74:1241–1250
DOI 10.1007/s00280-014-2602-x

ORIGINAL ARTICLE

Phase I study of intravenously administered ATI-1123, a liposomal docetaxel formulation in patients with advanced solid tumors

Devalingam Mahalingam · John J. Nemunaitis · Laeeq Malik · John Sarantopoulos · Steven Weitman · Kamalesh Sankhala · Jessica Hart · Ahmed Kousba · Nicole S. Gallegos · Gavin Anderson · John Charles · Jon M. Rogers · Neil N. Senzer · Alain C. Mita

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Abstract
Purpose ATI-1123 is a liposomal formulation of docetaxel and may be administered without the premedications and hypersensitivity reactions. This Phase I study examines the safety, tolerability, pharmacokinetics (PKs), and antitumor activity of ATI-1123.
Methods Patients with advanced solid malignancies received escalating doses of ATI-1123 intravenously over 1-h every 3 weeks. The dosing commenced using an accelerated titration design and was followed by a modified 3 + 3 Fibonacci schema to determine maximally tolerated dose (MTD). Plasma was analyzed for encapsulated/non-encapsulated docetaxel; PK analyses were performed using model independent method. Response was assessed using RECIST criteria.
Results In total, 29 patients received doses ranging from 15 to 110 mg/m^2. At 110 mg/m^2, two of six patients experienced dose-limiting toxicities including grade 3 stomatitis and febrile neutropenia. The 90 mg/m^2 cohort was expanded to ten patients and identified as the MTD. The most common adverse events were fatigue, nausea, neutropenia, anemia, anorexia, and diarrhea. ATI-1123 exhibited linear and dose proportional PKs. One patient with lung cancer had confirmed partial response, and stable disease was observed in 75 % patients.
Conclusions ATI-1123 demonstrated an acceptable tolerability and favorable PK profile in patients with solid tumors. Our results provide support for Phase II trials to determine the antitumor activity of this drug.

Keywords ATI-1123 · Docetaxel · Safety · Tolerability · Pharmacokinetics

Introduction

Docetaxel is an antimitotic agent which binds to the beta subunit of tubulin and causes stabilization of tubulin polymerization. This stabilization results in cell cycle arrest at the G_2/M phase, thus inhibiting mitosis [1]. It is a poorly water soluble semisynthetic taxane analogue, commonly used in the treatment of a variety of solid tumors including head and neck, non-small cell lung, prostate, breast, and gastric cancer [2–4]. The current recommended regimen for docetaxel is 60–100 mg/m^2 administered over 1-h every 3 weeks, depending upon the indication [5].
Taxotere® is the standard formulation of docetaxel with well-established safety and efficacy when administered in 3-week cycles [6]. Because of its poor water solubility, it is formulated with solvents that can potentially contribute to treatment-related adverse events such as hypersensitivity reaction. Current docetaxel and other taxane formulations often complicate drug delivery and can alter both the PK and toxicity profiles. These problematic issues have spurred

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Azaya Therapeutics, Inc., San Antonio, TX, USA

J. M. Rogers
ResearchPoint, Austin, TX, USA

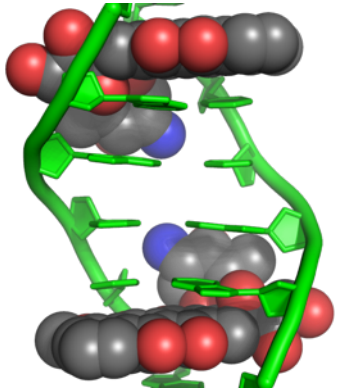
Springer

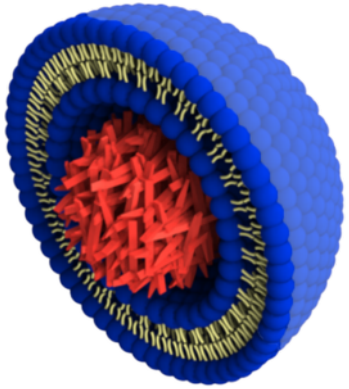
Reference: Mahalingham et al 2014

DoxoPLUS™ is a Generic of CAELYX®

Overview

- Doxorubicin (Adriamycin) is an anthracycline topoisomerase II inhibitor
  - Acts via DNA intercalation
  - Based upon a bacterial product (Streptomyces)
- Indications include breast cancer, bladder cancer, Kaposi's sarcoma, lymphoma, and acute lymphocytic leukemia
- Associated with well-known risk of dose-dependent cardiotoxicity and development of congestive heart failure
- PEGylated liposomal doxorubicin (CAELYX®) is the clinically preferred formulation with substantially lower cardiotoxicity than non-liposomal doxorubicin
- DoxoPLUS is designed as a complex generic version of CAELYX®
  - EMA Scientific Advice received
  - Clinical study completed demonstrating bioequivalence to CAELYX®
  - 18 months of development remaining to submit MAA to EMA





PLUS™ THERAPEUTICS

DoxoPLUS™ Clinical Bioequivalence

Study Design

- Single-blind, randomized (1:1) multi-center (US, Canada, Ukraine), two-way crossover study
- Patients with ovarian cancer that had progressed or recurred following platinum-based therapy
- 2 sequences of intravenous infusion at 1 mg/min once every 28 days

Sequence	Day 1, Cycle 1	Day 1, Cycle 2
A	50 mg/m^2 CAELYX	50 mg/m^2 CAELYX
B	50 mg/m^2 DoxoPLUS	50 mg/m^2 DoxoPLUS

- Key Pharmacokinetic Endpoints
  - Area under the plasma concentration versus time curve
    - Time 0 to last measurable concentration (AUC_{0-t})
    - Time 0 to infinity (AUC_{0-inf})
  - Maximum observed drug concentration (C_{max})
  - Time to maximum drug concentration (t_{max})
  - Apparent first order terminal elimination half-life ($t_{1/2}$)

Results

Analysis of 44 subjects dosed with EU-sourced CAELYX®

PK Parameter	CAELYX (LSGM)	DoxoPLUS™ (LSGM)	Bioequivalent*
Encapsulated Doxorubicin			
C_{max}	47,200	42,400	Yes
AUC_{0-t}	4,280,000	3,690,000	Yes
AUC_{0-inf}	5,040,000	4,400,000	Yes
Free Doxorubicin			
C_{max}	3,090	3,120	Yes
AUC_{0-t}	180,000	176,000	Yes
AUC_{0-inf}	230,000	226,000	Yes
Doxorubicinol			
C_{max}	3.36	2.99	Yes
AUC_{0-t}	489	442	Yes

*Confidence intervals within the target range of 80-125%

PLUS™ THERAPEUTICS

Capitalization Summary

Select Data (as of 03/31/20)	
Cash	$16.1M
Common Shares Outstanding	3,880,588
Series U warrants	3,520,000
Senior Term Loan (matures 2024) *	$4.3M

* As of May 14, 2020, 10-Q public filing, $5M of principal was paid on April 1, 2020

PLUS™ THERAPEUTICS

2020 Anticipated Milestones

- ✓ Pipeline expansion: RNL technology, new drugs in-licensed for pipeline
- ✓ Complete restructure term loan
- ✓ Close RNL in-licensing transaction
- + Optimize regulatory and clinical program for RNL glioblastoma, FDA feedback
- + Complete enrollment & report data from RNL glioblastoma Phase I dose finding trial
- + Phase II/pivotal trial plan for RNL glioblastoma
- + IND enabling studies for follow on asset
- + Potential acquisition, in-license new drug development candidates
- + Partner RNL, DocePLUS™ & DoxoPLUS™ assets

PLUS™ THERAPEUTICS

Corporate Information

+ Headquarters: Austin
+ Offices: Austin, San Antonio Texas
+ Nasdaq Symbol: PSTV
+ Website: plustherapeutics.com