

Corporate Presentation April 22, 2020

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# **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 cost 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.



# A New Oncology Focused Company

### + 'PLUS' is our cost-effective oncology development model:

- + Novel delivery technology combined with clinically or commercially proven APIs to create innovative therapies for patients
- + Versatile liposomal nanotechnology platform:
  - + Improves pharmacokinetics, distribution and uptake of numerous active pharmaceutical ingredients
- + Radionucleotide NanoLiposome (RNL<sup>™</sup>) platform:
  - + Facilitates incorporation of novel radionuclides into liposomal nanoscale drug formulations
- + Product development threshold:

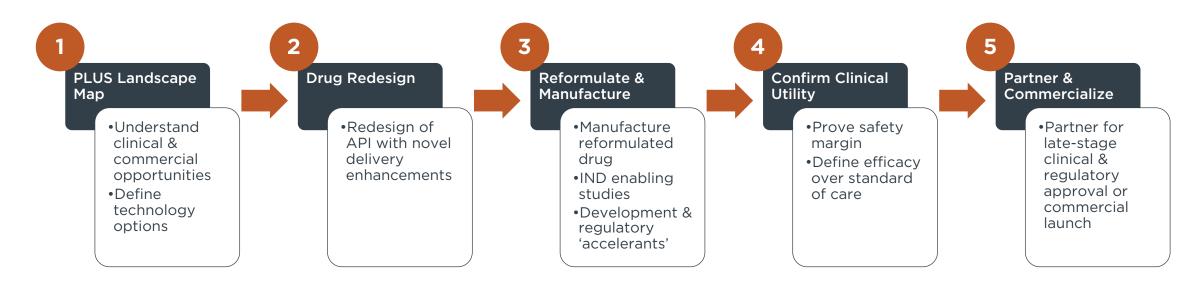
THERAPEUTICS

+ Clinical and late preclinical candidates addressing significant unmet/underserved needs each with global annual revenue potential exceeding \$250M with development 'accelerants'



# The PLUS Development/Acquisition Model







### March 2020: PLUS Licenses Novel Brain Cancer Therapy

### Rationale

- + Create long-term value through a substantially expanded and strengthened new drug pipeline
- + Create new near-term development milestones through the addition of Rhenium nanoliposomes for the treatment of recurrent glioblastoma
- + Leverage extensive proof-of-concept data in other disease targets to advance new product candidates into clinical trials

### Key Terms

- + Plus shall provide \$400K in cash and \$300K in Plus common stock at closing
- + Plus to make development and sales\* milestone payments of up to \$136.5M
- + Plus to pay a variable, single-digit royalty on US and European sales\*

**NIH/NCI** Funding 2019-2024 \$3.7M

#### **Clinical Sites**

UT Health San Antonio UT Southwestern **MD** Anderson

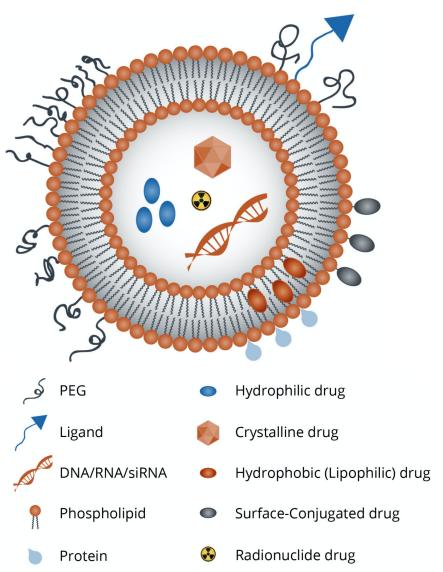
#### **Development Team**

Andrew Brenner, MD PhD Neuro Oncology William Phillips, MD Nuclear Medicine Ande Bao, PhD Radiation Physics



# Versatile & Valuable Nanotechnology Platform

- + Nexus of 2 Large Market Opportunities
  - Liposome-encapsulated drugs for cancer and other indications generated ~ \$2B in global sales in 2019\*
  - Therapeutic radionuclides achieved ~ \$700M in global sales in 2018\*
- + Current Development Focus
  - Nanoscale liposome-encapsulated radionuclides & cytotoxics
- + Proprietary
  - + U.S. & international patent protection







# Capabilities & Experience

- + Decades of drug, nanotechnology, and combination product development experience
- + Management team with successful track record clinical trials design & execution and launching novel products in the U.S. and internationally
- + A fully GMP-compliant, validated, state-of-the-art, U.S. development and manufacturing facility supported by an ICH-compliant Quality Management System
- + A 10,000 square foot facility with commercial scale negative pressure manufacturing suites with ISO Class 7 and 8 cleanrooms, onsite WFI and full handling capability for hazardous APIs
- + A dedicated analytical chemistry development and validation lab

# **Expanding Clinical Pipeline**



### RNL™

Proprietary Innovative BMEDA-Chelated Rhenium NanoLiposome



### DocePLUS™

Proprietary Innovative Albumin-Stabilized PEGylated Liposomal Docetaxel\*

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



# **Seeing Unlimited Possibilities** GIVING PROVEN THERAPIES NEW LIFE



# **Medical Radionuclides**

#### **Reactor isotopes** Cyclotron isotopes molybdeen-99 indium-111 diagnosis of diseases - e.g. heart failure, diagnoses, investigations of cancer - using Technetium-99m the brain and colon xenon-133 iodine-123 lung ventilation studies diagnosis of thyroid function holmium-166 thallium-201 therapy of e.g. liver tumours detecting cardiac conditions lutetium-177 therapy of e.g. neuroendocrine rubidium-82 tumours detecting cardiac conditions iodine-125 and iodine-131 gallium-67 therapy of prostate cancer and diagnosis of infections and thyroid conditions inflammation iridium-192 therapy of cervical, prostate, Type of isotope lung, breast and skin cancer description therapy strontium-89 pain management in bone cancer therapy & diagnosis yttrium-90 diagnosis therapy of liver cancer and rheumatic conditions

THERAPEUTICS

**Broad Diagnostic/Therapeutic Applications** 

### **Radiotherapeutics:** Double-Digit Growth



- + Increased PET/SPECT scanner installations globally
- + Supply chain consolidation
- + Negligible risk with radiopharmaceuticals

- Stringent FDA regulatory quidelines
- Demand-Supply gap of nuclear medicine physician

# Radiotherapeutics

### **Continued Investment and Proven Adoption**

- + 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<sup>®</sup> (radium Ra 223 dichloride) for prostate cancer; XOFIGO<sup>®</sup> achieves global sales of \$414M in 2018

### **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



# **Rhenium (Re) Is An Established Therapeutic**

#### Ideal Radionuclide For The Treatment Of Solid Tumors



- + Produced in nuclear reactor
- Isotope emits both therapeutic beta particles and gamma photon used for imaging
- + Approved product in Europe for the palliative treatment of bone pain from metastases
- + Distinctive and uniquely attractive therapeutic radionuclide
- Seamless integration in current hospital nuclear medicine workflows

Radionuclide	Annual WW Procedures
Tc-99m	35,000,000
1-131	1,000,000
Ir-192	120,000
Xe-133	100,000
I-125	27,000
Sr/ <b>Re</b> /Sm	20,000
Y-90	20,000
Lu-177	15,000
Ra-223	10,000
Alpha Emitters	2,000
Ho-166	400



### Therapeutic Construct: Novel Rhenium NanoLiposome (RNL<sup>™</sup>)

<sup>186</sup> Rhenium	<ul> <li>+ Dual emitter- therapeutic beta particle &amp; quantitative imaging photon to determine <i>in vivo</i> distribution</li> <li>+ Ideal isotopic properties- tumor radiation distribution 2-4mm &amp; 90-hour half-life maximizes tumor killing &amp; minimizes injury to normal tissue</li> </ul>
BMEDA- Isotopic Chelator	+ Versatile & proprietary small molecule + Required to form stable nanoliposome with Rhenium or other isotopes
NanoLiposome	+Liposome construct of ~100 nm diameter increases time of <sup>186</sup> Rhenium on the tumor +Facilitates delivery several hundred Gy to tumor
Convection Enhanced Delivery (CED)	<ul> <li>+ Most effective method of local delivery using both hydrostatic pressure &amp; time to fully distribute agents</li> <li>+ Micro-field therapy can cover entire tumor bed &amp; local tumor infiltration</li> </ul>



# **Standing Up to Brain Cancer** DEFYING ODDS ONE PATIENT AT A TIME



# **Glioblastoma: A Death Sentence**

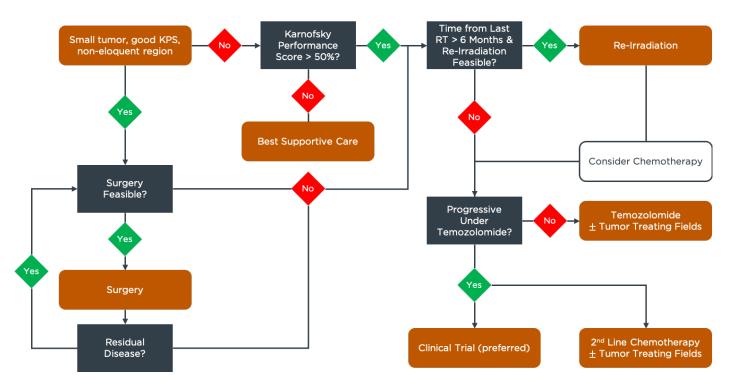


- Glioblastoma is a rare, incurable, and fatal brain cancer characterized by a rapidly growing and spreading malignant tumor
- Following an aggressive frontline multi-modality and interdisciplinary therapeutic approach, some tumor cells survive and cause tumor recurrence, which is inevitable
- Overall survival after the first recurrence is very low

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# Recurrent Glioblastoma Treatment: No Consensus or Compelling Options

- + Tumor recurrence is the norm
- Standards of care in tumor recurrence are less well-defined than for primary tumors
- Only 1 new therapy FDA approved since 2011
- External beam radiation is an essential component of standard treatment, but is limited by toxicity at doses > 80 Gy
- Patients and providers are seeking new treatment options for recurrent glioblastoma with improved safety and efficacy





# **RNL<sup>™</sup> for Recurrent Glioblastoma: Rationale**

### Many Potential Advantages Over Standard of Care, External Beam Radiation

- + Retention: unique method of trapping rhenium within the nanoliposome, thereby facilitating radioisotope retention within the tissue
- + Targeting: glial originating cells of the tumor retain their phagocytic ability and actively ingest the nanoliposomes, resulting in specific targeting of glioblastoma cells
- + Coverage: ability to treat the whole tumor, enhanced by rhenium's 2-4 mm average path length, equivalent to 80 160 cell diameters
- + Delivery: uses image-guided convection-enhanced local drug delivery that bypasses the blood-brain barrier
- + Dosing: administer much higher radiation absorbed doses to patients (perhaps 20x) which may result in markedly improved survival without compromising safety



### **RNL<sup>™</sup> vs. External Beam Radiation Therapy (EBRT)**

#### Rhenium NanoLiposome (RNL<sup>™</sup>)

- + Delivers a high dose of radiation directly to the tumor while sparing normal, healthy brain tissue
- + Stays at the tumor for several days
- + Effect lasts for several days and then dissipates
- No serious adverse events observed todate
- + Local, direct administration of beta emitters have the potential to dramatically widen the therapeutic window, increase delivered dose, and extend survival time

#### **External Beam Radiation Therapy**

- + Intended to treat cancer and ease cancer symptoms
- + Decades of successful use
- For primary glioblastoma, radiation is the most effective 'survival contribution' to combined therapy (5 months) compared to chemotherapy (2.5 months) and Tumor Treating Fields (3 months)
- + The therapeutic window for external beam radiation is limited by increasing late normal tissue damage



### **RNL<sup>™</sup>: Key Advantages Over EBRT in Recurrent Glioblastoma**

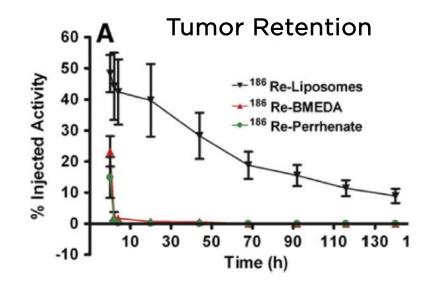
Feature	External Beam Radiation Therapy (EBRT)	RNL™
Maximum Safe Dose	36 - 42 Gy	At least 500 Gy
Treatment Duration	5X week over ~4 weeks	Single 4-day hospitalization
Dosage Control	Limited to enhancing tumor	Able to more effectively treat tumor margins
Safety profile	4 - 10% adverse event rate	Limited toxicity
Versatility	None	Possible combinations
Monitoring	None	Able to verify successful delivery with SPECT scan



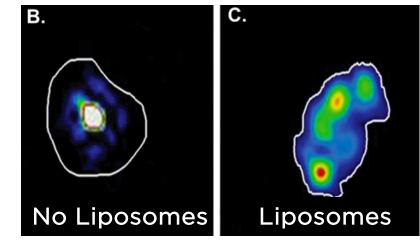
### **RNL<sup>™</sup>: Prolonged and Complete Tumor Coverage**

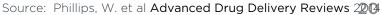
Liposomal encapsulation fundamentally changes both the **retention** within the tumor and the **dispersion** of the drug product

- Retention- unencapsulated rhenium is rapidly cleared from the tumor (A: red and green lines) & encapsulated rhenium persists in the tumor (A: black line).
- Dispersion- unencapsulated rhenium does not spread when injected and is (B) & encapsulated rhenium persists in the tumor with better distribution (C).



#### Tumor Dispersion







### **RNL<sup>™</sup>: Dramatic Survival Benefit in Rodent Studies**

Preclinical studies showed subjects tolerated absorbed RNL<sup>™</sup> radiation doses 30 times greater than that given by conventional external beam radiation

- + RNL<sup>™</sup> in 2 models of glioblastoma (A: U87 and B: U251) showed marked prolongation of animal survival
- Many animals showed no evidence of residual tumor on necropsy

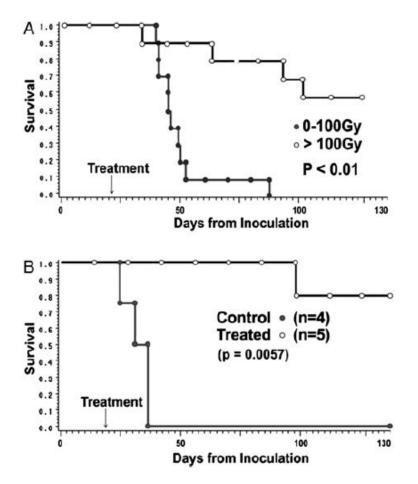
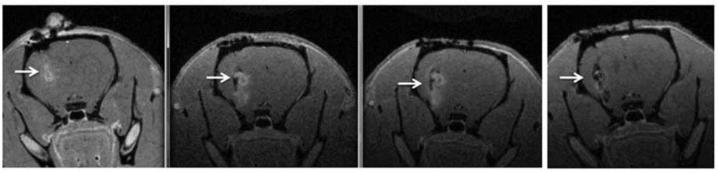


Fig. 6. Animal survival (A) from rats bearing U87 xenografts as a function of treatment of less than or greater than 100 Gy and (B) from animals bearing U251 xenografts.

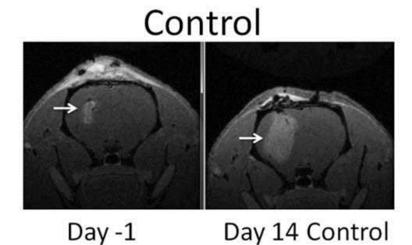


### **RNL<sup>™</sup>: Tumor Regression In Rodent Brain Tumors by MRI**

### <sup>186</sup>Re-Liposome Treatment



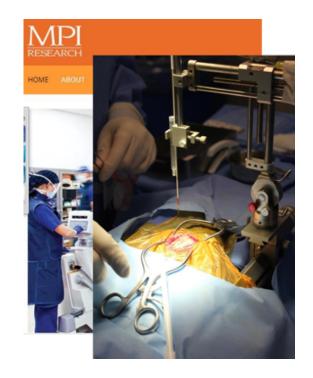
Day -1 Day 14 Post-Tx Day 28 Post-Tx Day 70 Post-Tx





### **RNL<sup>™</sup>: Safety Confirmed in GLP Toxicology Study**

- + Intracranial administration of 1, 3.5 or 6 mCi RNL<sup>™</sup> or control nanoliposomes produced no significant test article related 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 6 mCi RNL<sup>™</sup> and an absorbed dose of 360 Gy





### **RNL<sup>™</sup>: Enrolling Phase 1 Clinical Trial (NCT01906385)**

Multi-center, sequential cohort, open-label, volume and dose finding study of the safety, tolerability, and distribution of <sup>186</sup>RNL given by convection enhanced delivery to patients with recurrent or progressive malignant glioma after standard surgical, radiation, and/or chemotherapy treatment

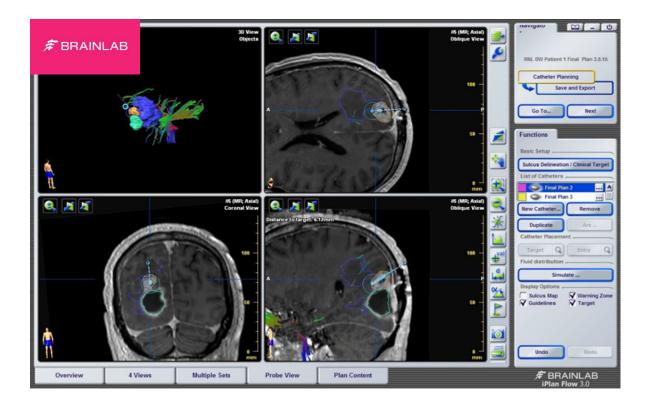
- + U.S. FDA IND approved
- + 13 patients with recurrent glioblastoma treated with RNL™ to-date; currently enrolling in cohort 5
- Absorbed doses up to 517 Gy have been delivered; dose is 10X to 15X what is typically delivered by external beam radiation therapy (EBRT)
- No treatment related adverse events higher than grade 1 have been encountered to-date -- appears to be very safe
- + Early signals of efficacy survival in first 2 patients > 2 years
- + Goal is to complete enrollment in 2020
- + Supported by a \$3.7M NIH/NCI R01 grant through Phase 2



# **Pre-Operative Treatment Planning**

PreOp	Day 1	$\setminus$ Day 2	∖ Day 3
<ul> <li>Surgical</li></ul>	• Catheter	<ul> <li>         •RNL™</li></ul>	<ul> <li>Patient</li> <li>Discharge</li> </ul>
Planning	Placement	Infusion	

- In silico planning of surgical placement for 1 to 4 catheters to 'cover' tumor
- + Uses MRI and CT scan information to calculate ideal catheter trajectory, number and depth to avoid critical brain structures & fully cover tumor
- + Predictive of distribution volume of RNL<sup>™</sup> in and around the tumor





# **Day 1: Catheter Insertion**



- + Patient admitted to hospital and OR
- Patient is secured in the stereotactic surgical system to obtain accurate geospatial positioning
- + Using the coordinates determined by the preoperative *in silico* surgical planning, 1 to 4 catheters are inserted into the tumor
- + Patient remains in the hospital for observation and to ensure proper catheter positioning

### **Stereotactic System**



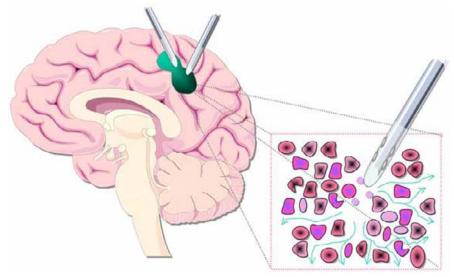


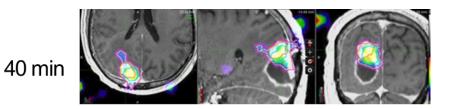


# Day 2: RNL<sup>™</sup> Infusion



- + RNL<sup>™</sup> is administered by convection enhanced delivery (CED) over several hours
- + SPECT/CT scanning is used per protocol during infusions to confirm predicted dispersion of the RNL™
- + Catheter is removed after infusion



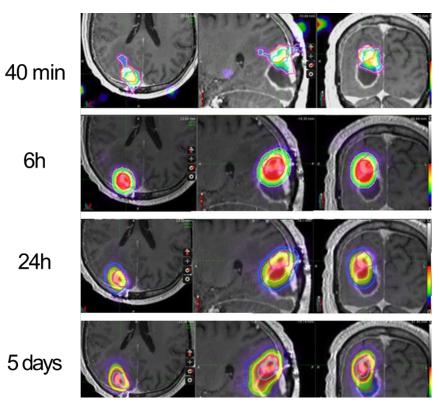


**PLUS** THERAPEUTICS

# Day 3: Discharge & Post-Operative Monitoring



- + Patient typically discharged within 48 hours after admission
- + No further procedures or hospitalizations are required
- + As shown in the adjacent scan, 5 days after the procedure, the RNL<sup>™</sup> remains largely restricted to the post-infusion distribution volume



Real-time Monitoring of Delivery & Retention



# **Example Case From Phase 1**

#### Patient 001

- No apparent clearance of radioactivity from the loco-regional location during the initial 72 hours
- Loco-regional retention was 96.4% of administered radioactivity on average from time 0 to 72 hours
- The average radiation absorbed dose to 4.3 ml of tumor volume was 143 Gy, which is much higher than typical external beam radiation therapy
- + Over 80% of the tumor volume effectively covered by the radiation at least out to 5 days
- + Patient survived 30 months (historically, median survival ~9 months)



### **RNL<sup>™</sup> Patient Benefits**

- + Convenience: single short hospital stay versus daily visits to the hospital for almost 4 weeks
- + Much higher radiation dose: compared to external beam radiation, which may translate into improved efficacy and prolonged survival

## **RNL<sup>™</sup> Development Plan**

	2020	2021	2023	2024	2025
Pilot/Phase 1	Complete Enrollment				
Manufacturing & Scaling	cGMP Product	Available			
Regulatory	Orphan & Accelerated Approval Process				
Planning for Pivotal	Pivotal Trial Prep	paration			
Anticipated Pivotal/Phase 2		Enroll 12-18 Mor	nths & Follow-Up 18 Months		

- + 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



### **RNL<sup>™</sup>: Indication Expansion Opportunities**

### Peritoneal Carcinomatosis

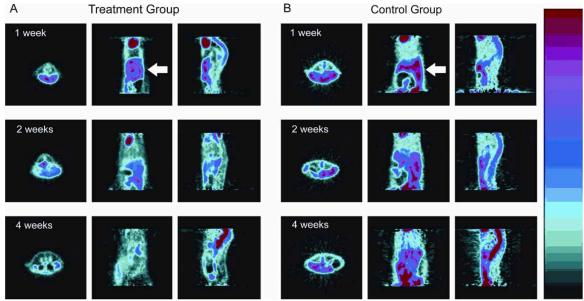
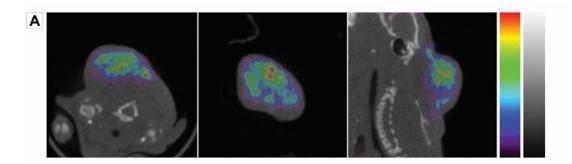


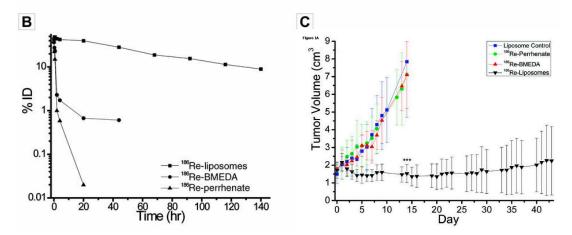
Figure 5. <sup>18</sup>F-FDG microPET images of the peritoneal cavity acquired 45 min post-injection at 1, 2, and 4 weeks post-treatment. (A) Corresponding transverse, coronal, and sagittal slices (left to right) of peritoneal cavity (arrow) in treatment group. The treatment group shows a gradual decrease in peritoneal <sup>18</sup>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 <sup>18</sup>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.

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### **RNL<sup>™</sup>: Indication Expansion Opportunities**

### Head & Neck Squamous Cell Carcinoma





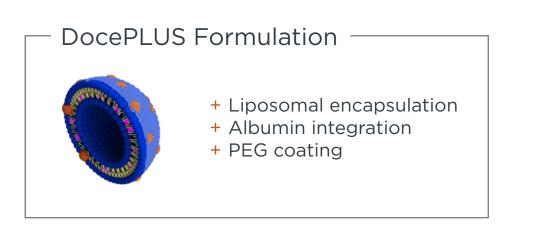


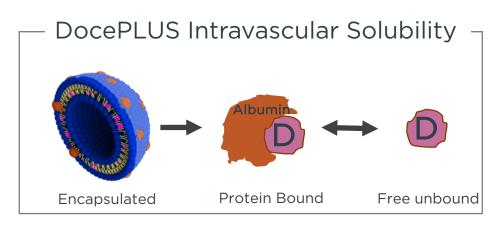


# Outlasting Lung Cancer MAKING EACH BREATH COUNT



# DocePLUS<sup>™</sup> Design Rationale, PK and PD





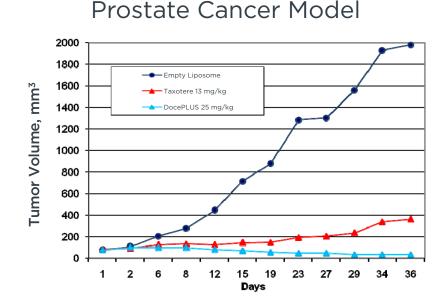
- + DocePLUS Liposomal Encapsulation
  - + Free unbound docetaxel distributed to tissues
  - + Encapsulated AUC 2-3X greater than unencapsulated<sup>1</sup>
  - + Intravascular depo & reduced clearance, lower  $V_{\rm ss}{}^2$
- + DocePLUS Albumin Integration
  - + Liposomal stabilization
  - + Docetaxel binds to albumin in plasma<sup>2</sup>
- + DocePLUS Polyethylene Glycol Coating (PEG)
  - + Reduced macrophage uptake
- + Compared to TAXOTERE®/Tween 80
  - + Surfactant increases unbound docetaxel, ~15%<sup>2</sup>
  - + DocePLUS free docetaxel C<sub>max</sub> 3.3x less TAXOTERE<sup>3</sup>
  - + AAG (α1-acid glycoprotein) acute phase reactant also responsible for plasma protein binding & variable in cancer patients<sup>2</sup>



Mahalingham et al 2014
 Loos et al., Clin Pharmacol Ther 2003; 74: 364-371
 NIH National Characterization Laboratory, NCL200911A
 Bruno et al., Am J Health-Syst Pharm Vol 54 Dec 15 1997 Suppl 2

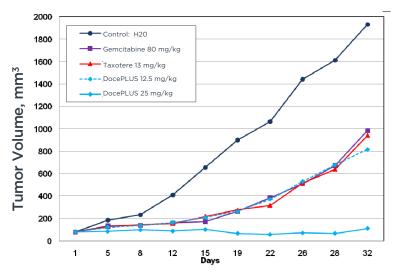
# **DocePLUS<sup>™</sup> Preclinical Findings**

- + Preclinical pharmacokinetic data support elevated AUC and C<sub>max</sub> of docetaxel for nanoparticle formulation
- + Biodistribution show preferential uptake to lung & liver
- + Immunodeficient xenograft tumor models in mice show DocePLUS<sup>™</sup> efficacy against a range of human tumor types
  - + Lung, prostate, pancreatic, mesothelioma



THERAPEUTICS

#### Pancreatic Cancer Model



# **DocePLUS<sup>™</sup> Phase 1 Study Key Findings**

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

#### + Safety

- + DocePLUS<sup>™</sup> 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 (nonencapsulated) docetaxel

#### + Efficacy

- + 22 of 29 patients (76%) experienced stable disease
- + 1 patient with NSCLC and previous exposure to docetaxel had confirmed partial response to DoxoPLUS™
- + 2 prostate cancer patients had PSA reduction >95%:
- 1 patient was progression free for 54 weeks 36

### THERAPEUTICS

Cancer Chemother Pharmacol (2014) 74:1241-1250 DOI 10 1007/-00280-014-2602-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

Received: 1 August 2014 / Accented: 1 October 2014 / Published online: 11 October 2014 © Springer-Verlag Berlin Heidelberg 2014

#### 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. 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/nonencapsulated 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/m2. At 110 mg/m2, two of six patients expe

rienced dose-limiting toxicities including grade 3 stomatitis and febrile neutropenia. The 90 mg/m2 cohort was

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A. Kousba MicroConstants, San Diego, CA, USA

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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.

Methods Patients with advanced solid malignancies Conclusions ATI-1123 demonstrated an acceptable tolreceived escalating doses of ATI-1123 intravenously over erability 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

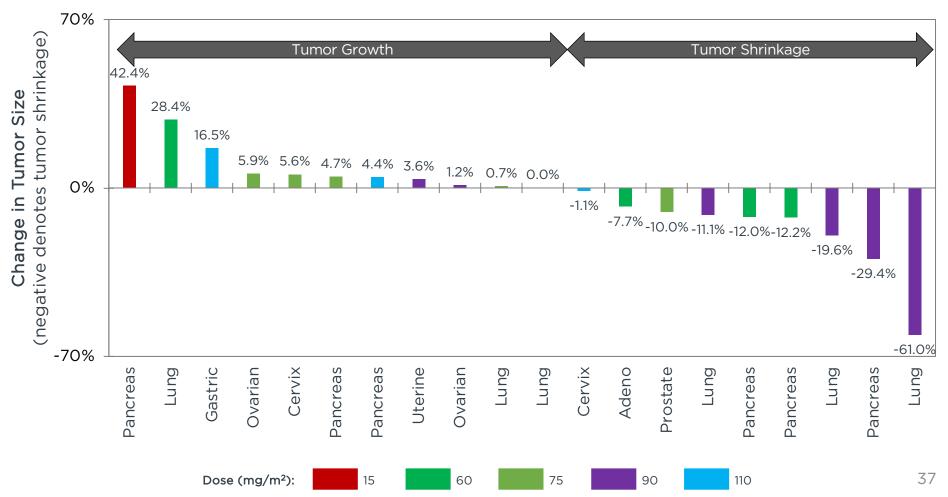
Introduction

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-/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/m2 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

# DocePLUS<sup>™</sup> Clinical Antitumor Activity

Patients in Order of % Change



THERAPEUTICS

# **Capitalization Summary**

Select Data (as of 12/31/19)			
Cash	\$17.5M		
Common Shares Outstanding	3,880,588		
Series U warrants	3,520,000		
Senior Term Loan (matures 2024) *	\$4.3M		



\* As of March 30, 2020, 8-K public filing

# **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<sup>™</sup> & DoxoPLUS<sup>™</sup> assets





#### **Corporate Information**

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



### Thank you!

