Issuer Free Writing Prospectus dated September 16, 2019 Filed pursuant to Rule 433 under the Securities Act of 1933 Relating to the Preliminary Prospectus dated September 16, 2019 Registration Statement No. 333-229485



This free writing prospectus relates to, and should be read together with, the preliminary prospectus dated September 16, 2019 included in Amendment No. 2 to the Registration Statement on Form S-1 (File No. 333-229485) relating to a public offering of the common stock, pre-funded warrants and warrants to purchase common stock of Plus Therapeutics, Inc. (the "Company").

The Company has filed a registration statement (including a prospectus) with the Securities and Exchange Commission (the "SEC") for the offering to which this communication relates. Before you invest, you should read the prospectus in the registration statement and other documents the Company has filed with the SEC for more complete information about the Company and this offering. You may get these documents for free by visiting EDGAR on the SEC Web site at Market and Market and



Investor Presentation
Nasdaq: PSTV

September 16, 2019

# Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These statements are based on our management's current beliefs, expectations and assumptions about future events, conditions and results and on information currently available to us.

All statements, other than statements of historical fact, included herein regarding our strategy, future operations, financial position, future revenues, projected costs, plans, prospects and objectives are forward-looking statements. Words such as "expect," "anticipate," "intend," "plan," "believe," "seek," "estimate," "think," "may," "could," "will," "would," "should," "continue," "potential," "likely," "opportunity" and similar expressions or variations of such words are intended to identify forward-looking statements, but are not the exclusive means of identifying forward-looking statements. Additionally, forward-looking statements include, without limitation, statements about our anticipated expenditures, including those related to pre-clinical and clinical trials and research studies and development, sales and marketing, and general and administrative expenses, the potential size of the market for our products, future development and/or expansion of our products in our markets, our ability to generate product or development revenues and the sources of such revenues, our ability to effectively manage our gross profit margins, our ability to obtain and maintain regulatory approvals, expectations as to our future performance, liquidity and capital resources, including our potential need for additional financing and the availability thereof, our ability to continue as a going concern, our ability to remain listed on the Nasdaq Capital Market, our ability to repay or refinance some or all of our outstanding indebtedness and our ability to raise capital in the future, and the potential enhancement of our cash position through development, marketing, and licensing arrangements. Such statements are based on currently available operating, financial and competitive information and are subject to various risks, uncertainties and assumptions that could cause actual results to differ materially from those anticipated or implied in our forward-looking statements due to a number of factors including, but not limited to,

Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to revise any forward-looking statements to reflect events or developments occurring after the date of this presentation, even if new information becomes available in the future.



-





- 'PLUS' is our cost effective pharmaceutical development model whereby novel delivery technology is combined with clinically and commercially-proven drugs to create innovative therapies for patients
- + Pipeline product candidates address significant unmet or substantially underserved medical needs and have a global annual revenue potential exceeding \$250M
- + DocePLUS™ -- proprietary innovative liposomal docetaxel formulation
  - + Potential benefits over comparative drugs
  - + Published U.S. Phase 1 clinical trial results
  - \* Received FDA orphan drug designation for small cell lung cancer
  - + Confirmed with FDA that 505(b)(2) NDA pathway appears to be an acceptable approach
  - + Preparing for Phase 2 clinical trial for small cell lung cancer
- + DoxoPLUS™ -- complex generic liposomal doxorubicin
  - + Completed clinical trial versus CAELYX® for EU bioequivalence
  - + cGMP validated facility for R&D, manufacturing, analytical testing
  - + Seeking divestiture to focus on innovative product candidates
- + Ongoing evaluation of new product candidates



## **Our Mission**

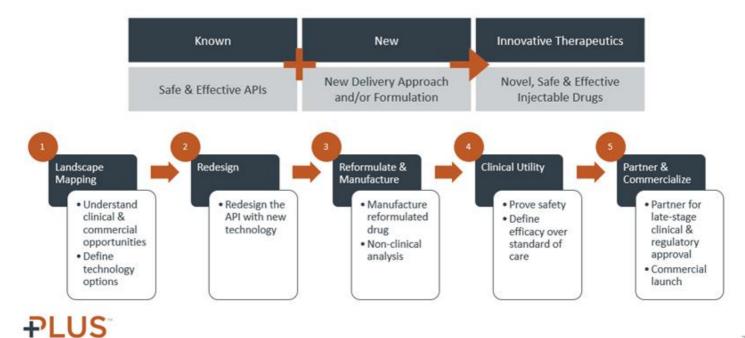
**Our Vision** 

We believe in the critical importance of discovering, developing, and delivering complex and innovative treatments for patients battling cancer and other life-threatening diseases.

We envision medicines that will drastically enhance clinical and economic outcomes for patients and providers and forever change the future of human health worldwide.



# The PLUS Development Model





# Capabilities and Experience

- Decades of drug, nanotechnology, and combination product development experience
- Management team with successful track record in completing clinical trials 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 cytotoxics
- + A dedicated analytical chemistry development and validation lab

# **Pipeline**



## DocePLUS™

Proprietary Innovative Albumin-Stabilized PEGylated Liposomal Docetaxel\*



## DoxoPLUS™

Complex Generic PEGylated Liposomal Doxorubicin Hydrochloride\*\*

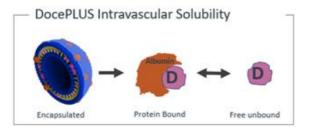
PROGRAM	CANCER TARGET	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	REGULATORY REVIEW	COMMERCIALIZATION RIGHTS
DocePLUS™	Small Cell Lung						PLUS - Global
PROGRAM	CANCER TARGET	PRECLINICAL	BIOEQUIVALENCE		REGULATORY REVIEW	COMMERCIALIZATION RIGHTS	
DoxoPLUS™	Breast Ovarian Multiple Myeloma Kaposi's Sarcoma						PLUS - Global



<sup>\*</sup> developed using a patented process
\*\* seeking asset divestiture

## DocePLUS™ Design Rationale, PK and PD







- Free unbound docetaxel distributed to tissues
- Encapsulated AUC 2-3X greater than unencapsulated<sup>1</sup>
- Intravascular depo & reduced clearance, lower V<sub>ss</sub><sup>2</sup>
- + 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%2
  - 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>



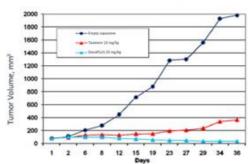
TAXOTERE is a registered trademark of Sanofi

1 Mahalingham et al 2014 2 Loos et al., Clin Pharmacol Ther 2003; 74: 364-371 3 NIH National Characterization Laboratory, NCL200911A 4 Bruno et al., Am J Health-Syst Pharm Vol 54 Dec 15 1997 Suppl 2

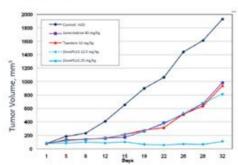
# DocePLUS™ Preclinical Findings

- 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™ efficacy against a range of human tumor types
  - + Lung, prostate, pancreatic, mesothelioma

### Prostate Cancer Model



## Pancreatic Cancer Model





# DocePLUS™ Phase 1 Study **Key Findings**

+ First-in-human, open-label, dose escalation (15-110 mg/m²) 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



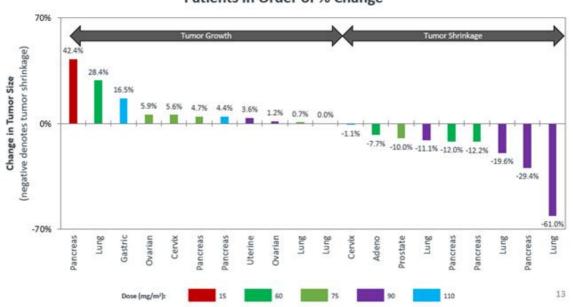
Dereilugum Viskulugum: John J. Noremelle: Long Visik: John Incestiquette: Union Welman Kantolic Baddule: Josius Hart: Gland Kantolic Nicolic S. Gallego: Garin Addresse: John Chai Jos H. Bagter: Josi V. Samer: John C. Hill.

12

Reference: Mahalingham et al 2019

# DocePLUS™ Clinical Antitumor Activity







# DocePLUS™ Development Plan

- + Underserved Market Opportunity
  - + Small Cell Lung Cancer; >\$250M annual revenue potential
- + Therapeutic redesign: known API PLUS new technology
  - + Docetaxel PLUS protein-stabilized PEGylated liposome encapsulation
- + Regulatory path
  - + Orphan, 505(b)(2)
- + Therapeutic reformulation: CMC, nonclinical
  - + Improved drug performance
- + Clinical
  - + Phase 1 complete
  - + Phase 2 ready
- + Commercial: partner or direct sales



# Initial Target: Small Cell Lung Cancer

- + Lung Cancer1
  - + 2<sup>nd</sup> most common cancer
  - + 14% of all new cancer cases
  - + Leading cause of cancer-related death in U.S.
  - + Diagnosed at median age of 70
- + 10-15% classified as Small Cell Lung Cancer<sup>1</sup>
  - + Smoking is #1 risk factor2
  - Low 5-year survival of 8-31%<sup>3</sup>
  - Most patients relapse following first-line therapy<sup>4</sup>
  - + HYCAMTIN® (topotecan), first FDA-approved in 1998, is indicated for platinum-sensitive patients who relapse >60 days after start of first-line therapy<sup>5</sup>



- 1 https://www.cancer.org/cancer/small-cell-lung-cancer/about/key-statistics.html
  2 https://www.cancer.org/cancer/small-cell-lung-cancer/causes-risks-prevention/risk-factors.html
  3 https://www.cancer.net/cancer-spes/lung-cancer-amall-cell/statistics
  4 https://ascopubs.org/doi/hulf/0.12003/0P.18.00204
  5 https://www.accessdata.fda.gov/drugsatfda\_docs/label/2018/020671s023lbl.pdf

HYCAMTIN is a registered trademark of Novartis







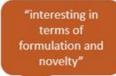
## Unmet Needs for Second-Line SCLC Treatment

- + DocePLUS: rationale for use in SCLC
  - + Biodistribution favorable for pulmonary delivery
  - + Phase I potential efficacy signal in lung cancer (NSCLC)
- + Single-Agent Chemotherapy with HYCAMTIN®
  - + Demonstrated activity in SCLC
  - In randomized clinical trial, key endpoints (ORR, DoR, TTP, OS) were not statistically improved over CAV treatment
  - Adverse reactions included neutropenia, anemia, and thrombocytopenia
  - Difficult dosing schedule: 1.5 mg/m<sup>2</sup> IV infusion over 30 minutes daily on days 1 to 5 of each 21-day cycle

HYCAMTIN is a registered trademark of Novartis

## DocePLUS™ Market Research

"fan of liposomal enveloping techniques"







In considering 10 solid tumors and 3 target product profiles, oncologists viewed SCLC as an attractive Phase 2 study indication

- + Low cure rate, rapid progression, low survival
- + Lack of effective treatment options
- For second-line, view current standard of care as toxic, inconvenient, and minimally efficacious
- + Expect shorter trial and easier patient recruitment (relative)

Oncologists also cited pancreatic cancer as an attractive target and described a high willingness to use DocePLUS™ if FDA-approved for this indication

- + Limited treatment options
- + Difficulties in achieving good results with new treatments



Source: PLUS THERAPEUTICS interviews of U.S. physicians and payers

# DocePLUS™ Proposed Differentiation in SCLC

#### Compared to HYCAMTIN®

- Convenient dosing schedule: IV infusion over 60 minutes on only day 1 of each 21-day cycle
- + Potential improved biodistribution to lung
- + Potential for improved safety & efficacy

#### Compared to TAXOTERE®

18

- Eliminates need for Tween 80 surfactant and associated with hypersensitivity reactions by encapsulating docetaxel in lipid bilayer of a liposome and albumin
- Potential improved pharmacokinetics & pharmacodynamics<sup>1,2,3</sup>
- + Potential for improved safety & efficacy

Mahalingham et al 2014
 Loos et al., Clin Pharmacol Ther 2003; 74: 364-371
 NIH National Characterization Laboratory, NCL200911A

HYCAMTIN is a registered trademark of Novartis TAXOTERE is a registered trademark of Sanofi





## Corporate Information

+ Headquarters: Austin

+ Offices: San Antonio, San Diego

Employees: 7 full-time

Nasdaq Symbol: PSTV

+ Website: plustherapeutics.com



# **Key Anticipated Milestones**

- + DocePLUS™ Phase 2 Clinical Trial in Small Cell Lung Cancer
  - + Q4 2019: FDA clinical trial protocol approval
  - + Q3 2020: 1st patient enrolled
  - + H2 2021: Patient enrollment complete
- + Pipeline opportunities
  - + Expand DocePLUS™ indications
  - + Acquire and/or in-license new drugs for niche and orphan markets
- + Divest DoxoPLUS™ complex generic asset



# Capitalization

Select Data †					
Cash	\$4.5M				
Common Shares Outstanding	443,117				
Preferred Shares Outstanding	4,540				
Senior Term Loan	\$9.3M				



† As of June 30, 2019