Shuttle Pharmaceuticals Holdings, Inc.

Shuttle Pharmaceuticals, Inc.
Shuttle Diagnostics, Inc.

Nasdaq: SHPH
Investor Presentation
Spring 2025

Forward Looking Statements

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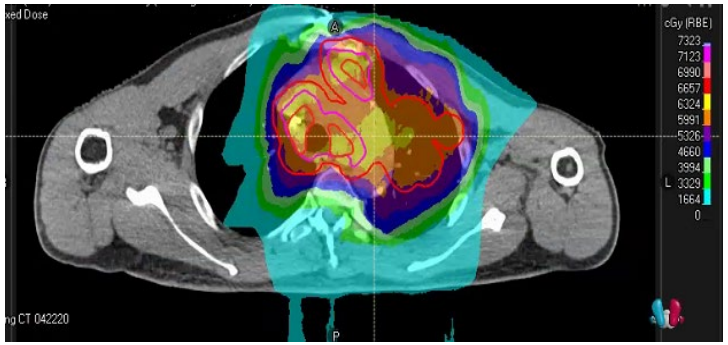
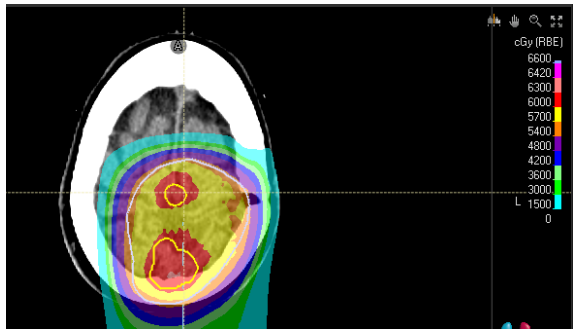
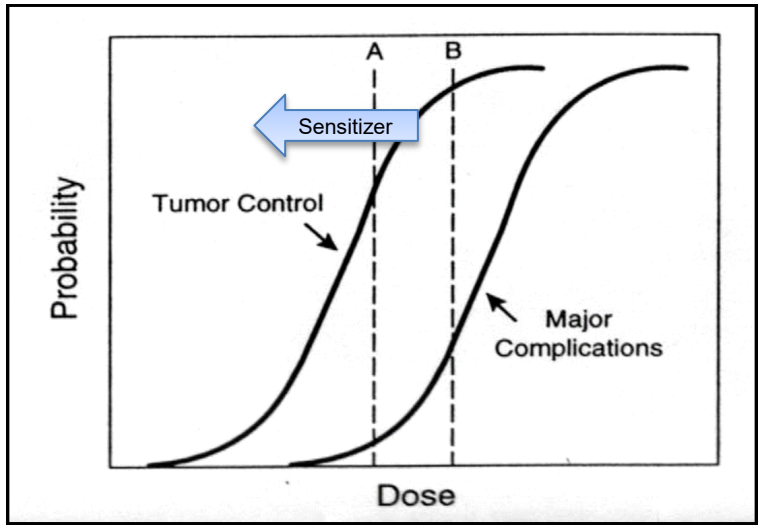
The Fundamental Problem of Radiation Therapy:

Cancers are surrounded by radiation sensitive, dose-limiting normal tissues







Sensitization of cancer cells to radiation therapy

- Radiation dose determines cancer curability
- Radiation therapy limitations are due to sensitive adjacent normal tissues
- Sensitizer drugs make cancer cells more sensitive to radiation therapy
- Currently available sensitizer drugs are mostly used “off-label”

Activation of the immune response augments post-RT tumor responses

- Radiation of cancers induces antigens and activates cellular immunity
- Pembrolizumab and Durvalumab immune therapies of lung cancers have shown improved responses after SBRT or after chemoradiation, respectively

Theranostics – Targeted diagnostics and therapeutics

- Metabolomics-based predictive biomarkers of radiation response
- PSMA-Ligand directed imaging (PET scanning)
- PSMA-Ligand directed radiopharmaceuticals and therapeutic agents

Company Overview: Cancer Treatment Using

Shuttle Pharma (Nasdaq: SHPH) is a clinical-stage pharmaceutical company, developing next generation drugs and diagnostics to improve outcomes for cancer patients treated with radiation therapy (RT).

Shuttle Pharmaceuticals Holdings, Inc. (SHPH, Nasdaq)

- Shuttle Pharmaceuticals, Inc.
- Shuttle Diagnostics, Inc.
  - Shuttle Dx (possible spinout)

Therapeutics

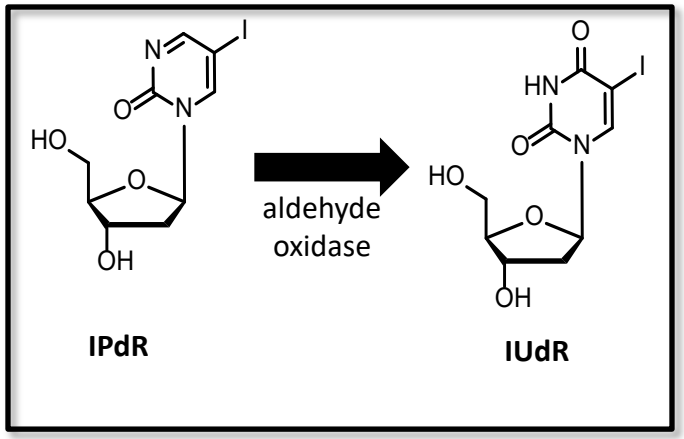
- **Ropidoxuridine** is a clinical stage, orally-administered cancer radiation sensitizer
- **SP-2-225** is a pre-clinical stage, selective HDAC6 inhibitor for innate post-RT immune system activation

Diagnostics

- **PC-RAD Test** is a predictive blood test of therapeutic outcomes to RT for organ-confined prostate cancers
- **PSMA-B ligand** is a theranostic molecule for diagnosis and therapy of metastatic prostate cancers

Therapeutics – How does Ropidoxuridine (IPdR) work?

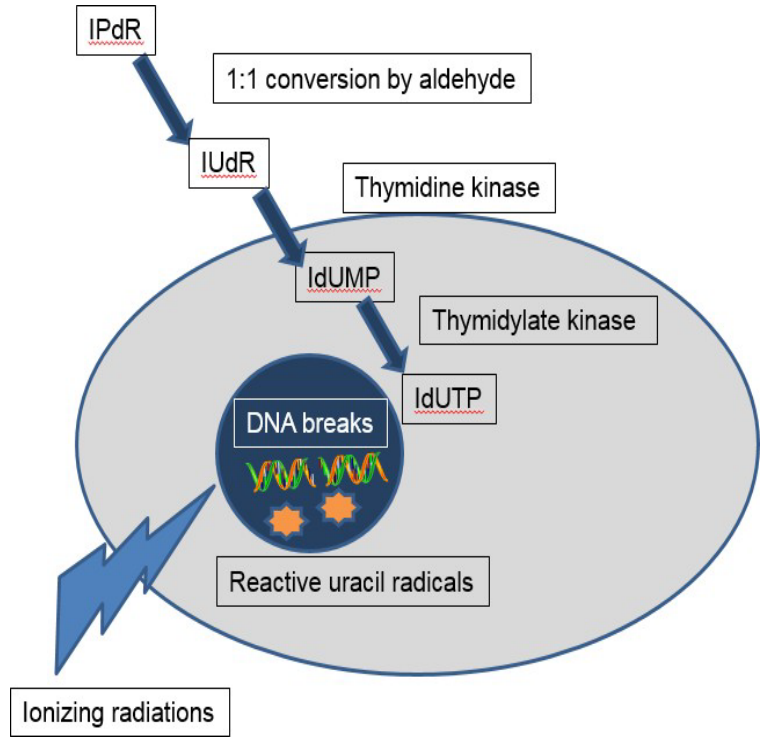
Ropidoxuridine (IPdR) is the prodrug of IUdR, a powerful radiation sensitizer, reported to improve clinical outcomes of patients treated for brain tumors and sarcomas in NIH supported Phase I/II clinical studies.



Tumor	Treatment	Median survival (Months)
Anaplastic astrocytomas (Grade 3 of 4)*	RT alone	24
	RT + IUdR	39
Glioblastoma Multiforme (Grade 4 of 4)**	RT alone	9
	RT + IUdR	15

Mechanism

After oral administration of Ropidoxuridine (IPdR), the prodrug is metabolized to IUdR, incorporates into the DNA of rapidly growing cancer cells and enhances RT induced DNA breaks by a free-radical mechanism.

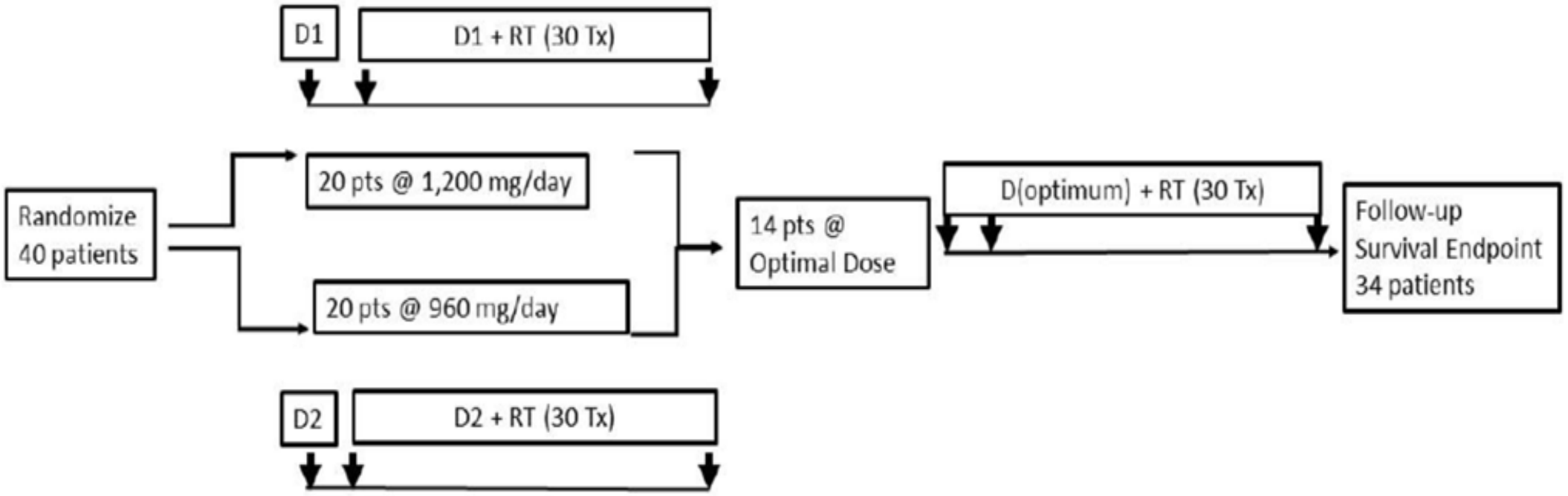


Comments and Observations

- **IUdR required constant infusion delivery**, subjecting patients to adverse events.
- **IPdR is an orally administered prodrug**, converted to IUdR for the sensitizer effect.
- **A Phase I and pharmacology study of Ropidoxuridine and RT,** funded by an NIH SBIR contract awarded to Shuttle Pharma with Brown University/Rhode Island Hospital as sub-contractor, identified the MTD of 1200 mg daily for 28 days, with 4 patients showing partial response, 9 stable disease, 1 progressive disease (Clin Cancer Res, 2019).

Ropidoxuridine (IPdR) – Phase II Clinical Trial

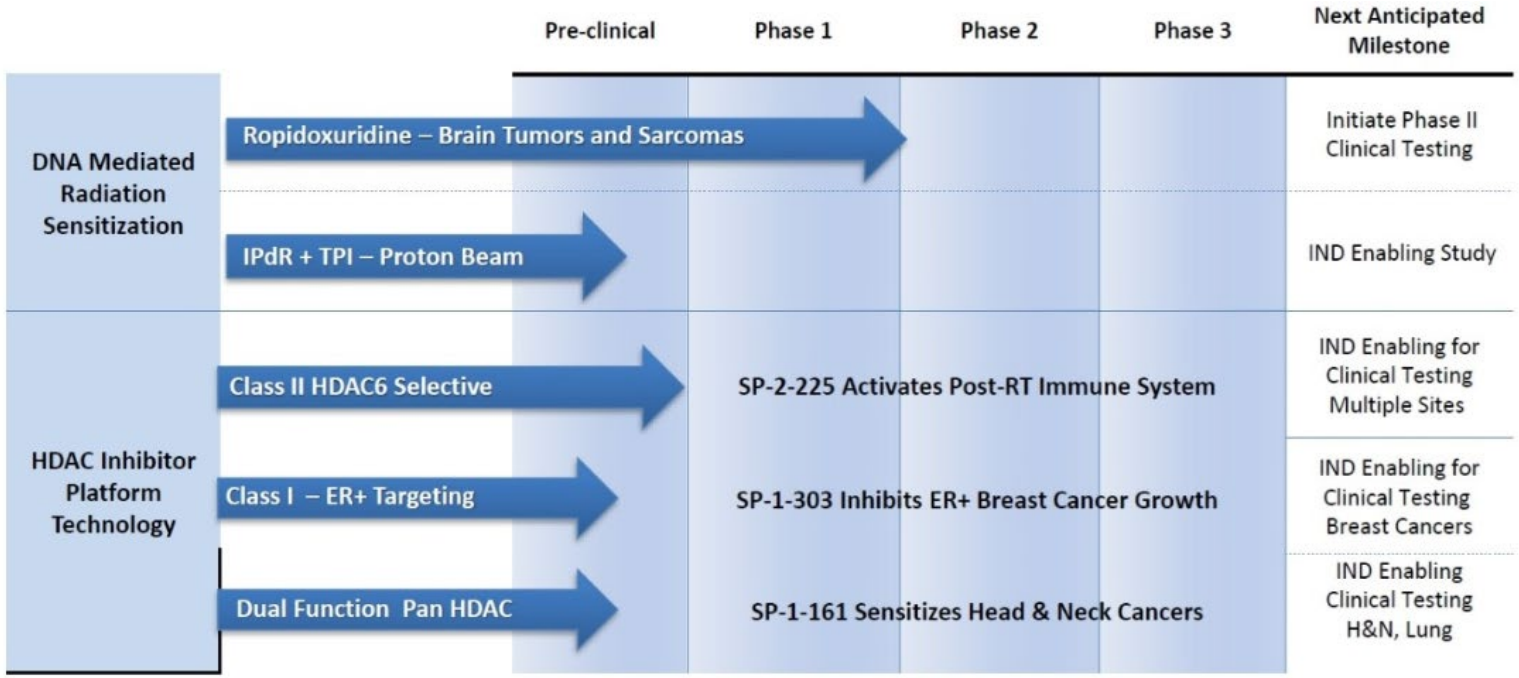
- **Phase II study of Ropidoxuridine + RT in IDH wild-type, methylation negative glioblastoma patients.**



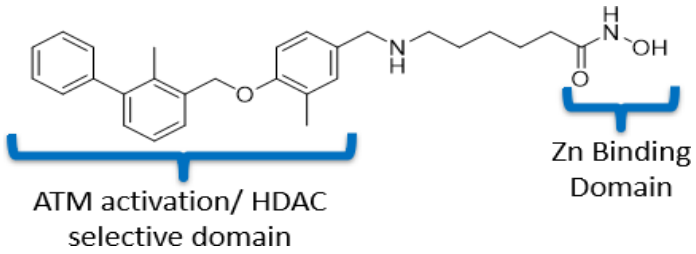
- **TCG GreenChem manufactured API, University of Iowa Pharmaceuticals formulated the drug product (capsules).**
- **Theradex Oncology provides CRO services for the FDA-approved, multi-institutional Phase II clinical trial.**
- **Clinical enrollment to date is 19 patients at 6 East Coast Cancer Centers.**
- **Results readout is anticipated to require 12 to 15 months.**

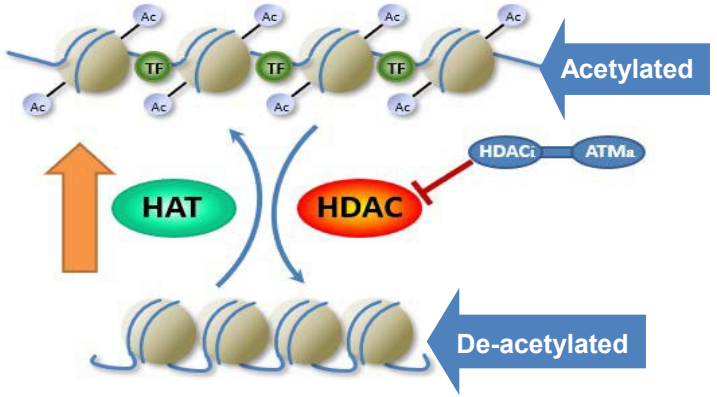
Therapeutics: Selective HDAC Inhibitor Development

Therapeutic Pipeline includes histone deacetylase inhibitors for post-RT immune stimulation and treatment of ER+ breast cancers.



Mechanism
HDAC inhibitors





Comments and Observations

- **Novel HDAC inhibitors - discovered and patented by Shuttle Pharma scientists.**
- **Candidate lead HDAC6 inhibitor (SP-2-225) for RT and immunotherapy treatment.**
- **Candidate Class I HDAC inhibitor (SP-1-303) for ER+ breast cancer treatment.**

Therapeutics: Clinical and Pre-clinical Development Strategies

1. **Clinical development of Ropidoxuridine & RT**
   - **Complete the Phase II clinical trial of Ropidoxuridine & RT in glioblastoma brain tumors**
   - **Prepare Ropidoxuridine and RT randomized Phase III clinical trial for full marketing approval**
   - **Support investigator-initiated clinical trials to expand clinical indications**

2. **Pre-clinical development of HDAC6 selective inhibitor SP-2-225**
   - **Scale-up manufacturing and formulation**
   - **Perform IND-enabling studies of SP-2-225**
   - **Advance Phase I & II clinical trials of SP-2-225 and RT for multiple cancer indications**

3. **Pre-clinical development of HDAC 1&3 selective inhibitor SP-1-303**
   - **Scale-up manufacturing and formulation**
   - **Perform IND-enabling studies of SP-1-303 for ER+ breast cancer treatment**
   - **Advance Phase I & II clinical trials of SP-1-303 in advanced breast cancers**

Diagnostics: Clinical Validation of the PC-Rad Test

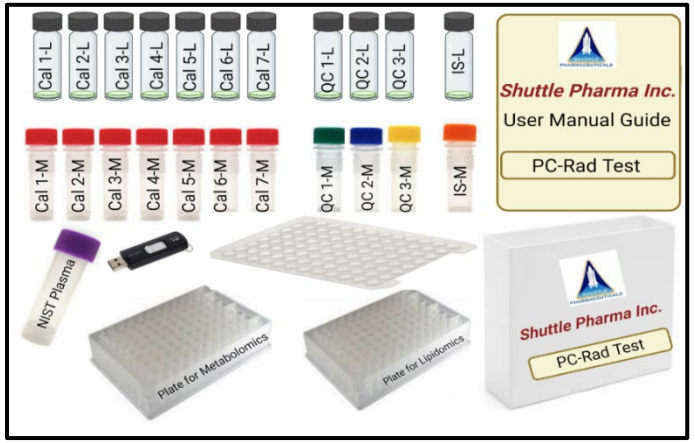
- **Market Opportunity: Predictive biomarkers for prostate cancers**
  - **~ 268,000 new prostate cancer cases** annually in the U.S. **(incidence)**
  - **~ 3,100,000** patients currently live with prostate cancer in the U.S. **(prevalence)**
  - **~ 66,000** patients with localized radiation (30%) receive RT for prostate cancer

- **Diagnostic tests predicting prognosis may help direct potential interventions.**
- **Global prostate cancer diagnostics market size was estimated at $ 8.56 billion in 2023.**
- **There is no currently available tests predictive of success of a specific treatment.**
- **Address the key unmet need for a minimally invasive diagnostic test to inform the clinician and patient of potential success of RT for prostate cancer treatment.**
- **The PC-Rad Test is a predictive pre-treatment blood test, measuring metabolite levels.**

Sources: American Cancer Society Facts & Figures, National Cancer Institute Cancer Statistics 2020
Clarivate Research; Prostate Cancer – Landscape & Forecast – Disease Landscape & Forecast, published January 2023
Grandview Research – Market Analysis Report - 2023

PC-Rad Test Kit Components

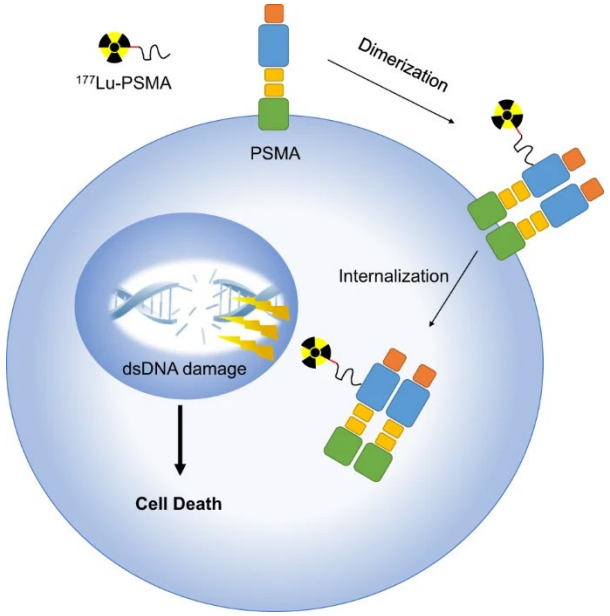
- **Calibrants for standard vials/ metabolomics and lipidomics**
- **QC and internal standards**
- **NIST Plasma reference standard**
- **User Manual Guide**
- **USB Stick with proprietary software to calculate score index**
- **2 x 96 well plate for sample preparation**
- **Pre-formatted mat/plate cover**



Diagnostics: Product Development – PSMA-B ligand

- **The prostate-specific membrane antigen (PSMA) is located on the outside membranes of prostate cancer cells.**
- **The PSMA ligand binds to PSMA, dimerizes, and is internalized into the cell. Radioactive molecules can be attached to the ligand.**
- **Theranostic radiopharmaceuticals are marketed for imaging (PET scanning) or treatment of patients with advanced PSMA–-positive metastatic castration-resistant prostate cancer.**

PSMA-B is a novel ligand invented by Shuttle Pharma scientists for use in prostate cancer treatment. Potential uses include diagnostic and therapeutic applications.



Adapted from: Radiotheranostics in advanced prostate cancer: Current and future directions. Jia AY, Kiess AP, Li Q, Antonarakis ES. Prostate Cancer Prostatic Dis. 2024.. PMID: 37069330.

Theranostics: PSMA ligand for diagnosis and treatment

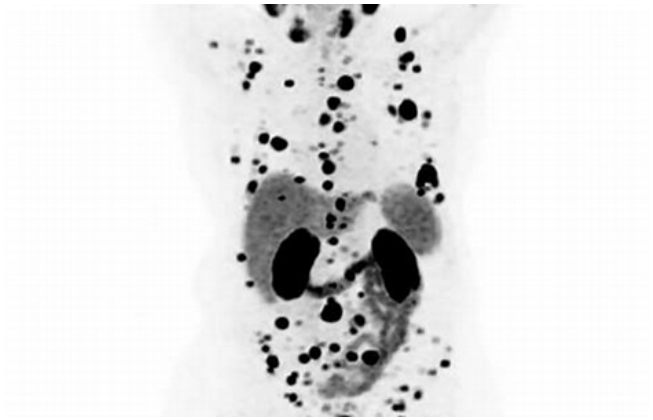
Market Opportunity: PSMA imaging and therapy

- The Global PSMA PET Imaging Market reached $ 1.5 billion in 2022 and is expected to reach $ 2.0 billion by 2030.
- PYLARIFY (piflufolastat F-18) is a radioactive diagnostic agent marketed by Lantheus for prostate cancer PET scanning.
- PLUVICTO (^{177}Lu-PSMA-617), is a radiopharmaceutical marketed by Novartis to treat adults with advanced PSMA–positive metastatic castration-resistant prostate cancer.

Shuttle Diagnostics: PSMA-B intellectual property

- PSMA-B is a novel molecule designed for boron proton capture and boron neutron capture therapy.
- PSMA-B has nanomolar affinity for PSMA as determined by enzyme inhibition.
- PSMA-B theranostic development for prostate cancer.

PET Scan
Widely metastatic prostate cancer



Source: Clarivate Research; Prostate Cancer – Landscape & Forecast – Disease Landscape & Forecast, published January 2023

Diagnostics: Clinical and Pre-clinical Development Strategies

1. Develop the PC-Rad Test intellectual property as a predictive diagnostics test

Predictive Biomarker for Prostate Cancer

- Validate the predictive assay in the context of use (COU) for FDA approval.
- Perform a muti-institutional clinical trial of the PC-RAD Test in patients undergoing RT as primary treatment for localized prostate cancer.

2. Develop PSMA-B intellectual property for theranostic applications

PSMA-B ligand evaluation for diagnosis and therapy

- Complete PSMA-B radiation sensitization studies with proton and neutron radiations.
- Determine radioisotope labelled PSMA-B imaging in animal models of prostate cancer
- Screen PSMA-B ligand-drug conjugates for targeted therapy of prostate cancer.
- IND-enabling studies of imaging and ligand-drug conjugates.
- Clinical translation (Phase I clinical trials) of imaging ligands and ligand-drug conjugates for prostate cancer management.

Shuttle Pharmaceuticals Holdings, Inc. - Intellectual Property

1. Ropidoxuridine (radiation sensitizers)

- Orphan disease designation, manufacturing technology, and method of use patent for the next generation IPdR/TPI formulation.

2. Selective HDAC inhibitors (radiation sensitizers/immune modulators)

- > 20 composition of matter patents in the U.S., Canada and Europe for novel HDAC inhibitors including HDAC6 (Class IIb) selective SP-2-225, HDAC 1 and 3 (Class I) selective HDAC inhibitor SP-1-303.
- All HDAC inhibitor patents are the Company's exclusive properties, invented or co-invented by Shuttle Pharma's scientists, no milestones or royalty payments are required.

3. PC-RAD Test (predictive biomarker)

- PCT patent application "Metabolomics-based diagnostic predictive biomarker". Exclusive license from Georgetown University.

4. PSMA-B (theranostic/diagnosis)

- PCT stage patent application for "Boron containing PSMA ligand for use in the treatment and diagnosis of prostate cancer." SHPH owned and exclusive license from inventors.
- Provisional patent application "PSMA-Targeted PARP Inhibitor Conjugates for Precision Cancer Therapy." SHPH owned and exclusive license from inventors.

Financial Overview

Shuttle Pharmaceuticals Cap Table		
Common Stock (as of 12/31/24)		4,076,567
March 2025 Offering:		
Common stock issued	1,340,921	
Pre-Funded Warrants	17,825,746	
Total		19,166,667
Convertible Bridge Note Shares		125,000
RSUs Vested		840,205
RSUs Outstanding		796,925
Warrants Outstanding		3,464,281
Pre-Funded Warrants Outstanding		1,826,000
Total Shares, Fully Diluted*		30,295,645

Capital Market Profile	
Exchange/Ticker	NASDAQ: SHPH
Closing Stock Price*	$0.265
52 Wk High/Low*	$0.23 - $4.71

* As of 4/15/2025

On March 13, 2025, Shuttle Pharma announced the closing of a $5.75 million underwritten offering (before deducting underwriting discounts and commissions and other offering expenses).

*As of March 31, 2025, excludes 3,127,404 shares potentially issuable for convertible bridge notes

Experienced Leadership Team

Anatoly Dritschilo, MD
Chairman of the Board of Directors, and Chief Scientific Officer

- Founder of Shuttle Pharma; Chairman, Board of Directors 2017
- Former Member, Board of Directors, Neopharm Inc. Chairman, Department of Radiation Medicine, Medical Director Georgetown University Hospital, interim Director, Lombardi Cancer, Georgetown University School of Medicine,
- Fellow ACR, NAI

Christopher Cooper
Interim Chief Executive Officer

- Appointed Interim-CEO March 2025
- President, CEO and Founder of First Towers & Fiber Corp. (2017-present)
- Former President, CEO and Founder of First Towers & Fiber Corp. (2010-2017)
- Former Corporate Consultant to various companies in the technology and resources sectors (1998-2010)
- MBA from Dowling College. BBA from Hofstra University.

Timothy J. Lorber, CPA
Chief Financial Officer

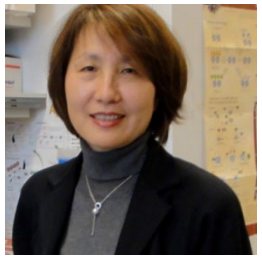
- CFO of Shuttle Pharma 2024
- CPA with >40 years financial experience
- Former Managing Director and Chief Accounting Officer Legg Mason, Inc.
- Audit Director Freddie Mac
- BA accounting, Loyola University

Peter Dritschilo, MBA
President & COO

- President & COO of Shuttle Pharma 2012
- CFO Shuttle Pharma
- (2012-2019
- Co-Founder Shuttle Pharma
- Radiation oncology administrator:
- Rad America, Inova Health
- MBA George Washington University

Michael Vander Hoek, MHSA
VP Regulatory

- VP Regulatory Shuttle Pharma 2012
- CFO Shuttle Pharma 2019 - 2024
- Former Administrative Director, Lombardi Cancer Center
- MHSA George Washington University



Mira Jung, PhD
Founder & Scientific Director

- Scientific Director of Shuttle Pharma 2012
- Co-Founder Shuttle Pharma 2012
- Radiation Biology, Georgetown University
- Professor of Radiation Medicine Georgetown University
- PD Molecular Biology University of Kansas

Tyvin Rich, MD
Chief Medical Officer

- Medical Officer of Shuttle Pharma 2019
- Radiation Oncology Training – Harvard, MGH
- Radiation Oncology faculty Harvard JCRT, MD Anderson Cancer Center, Radiation sensitizer clinical trials
- Chairman of Radiation Oncology, University of Virginia

THANK YOU

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