Shuttle Pharmaceuticals Holdings, Inc.

Nasdaq: SHPH

Investor Presentation

Fall 2024

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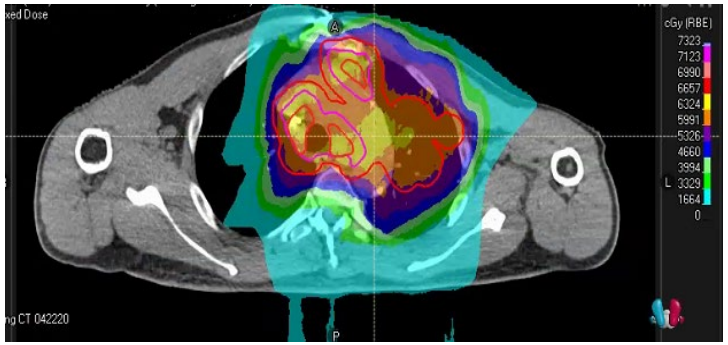
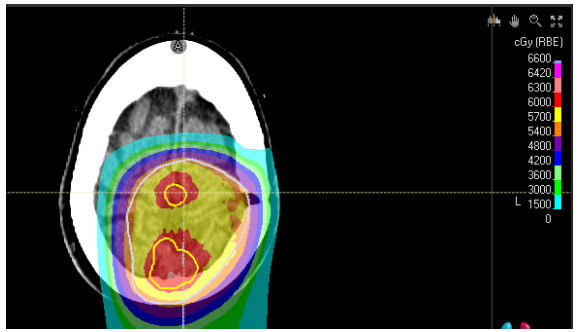
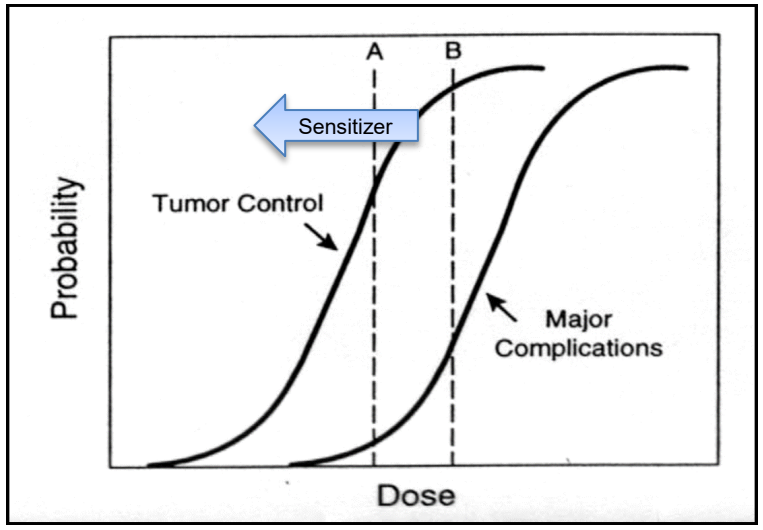
The Fundamental Problem of Radiation Therapy:

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







Sensitization of cancer cells to radiation therapy

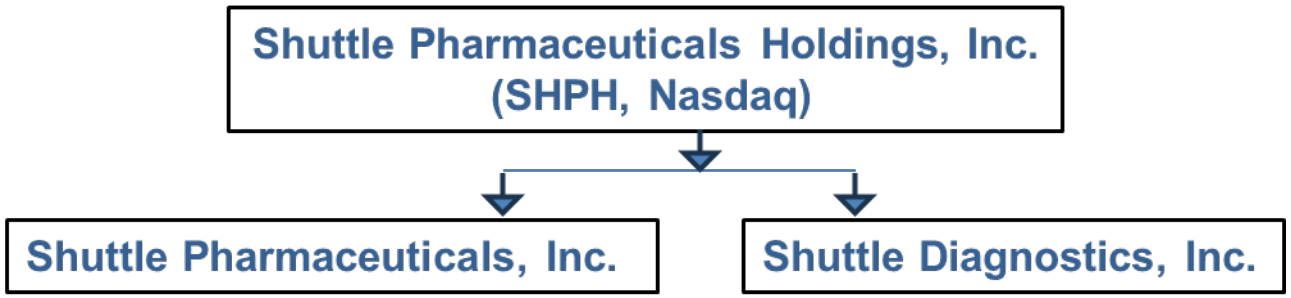
- The radiation dose determines cancer curability
- Adjacent normal tissues are dose-limiting
- Radiation sensitizers shift the dose-response to improve cancer control
- Currently available sensitizer drugs are mostly used “off-label”

Activation of the immune response augments post-RT tumor responses

- Radiation of cancers induces antigens and activates cellular immunity
- Pembrolizumab and Durvalumab immune therapies have shown improved responses in NSCLC after SBRT or after chemoradiation, respectively
- HDAC6 selective inhibitors enhance immune responses in pre-clinical models

Company Overview

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).



Therapeutics

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

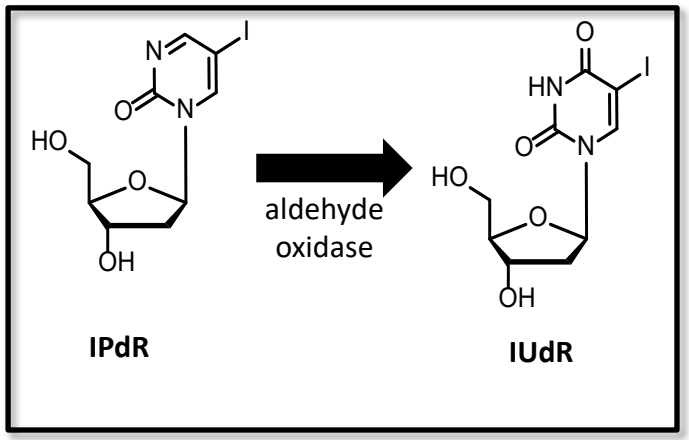
Diagnostics

- **PC-RAD Test** is a blood tests for predicting outcomes following RT for localized prostate cancer.
- **PSMA-B ligand** is a theranostic molecule offering diagnosis and therapeutics for metastatic prostate cancer.

Therapeutics – How does Ropidoxuridine (IPdR) work?

Ropidoxuridine (IPdR) is the prodrug of IUdR, a powerful radiation sensitizer. Following oral administration, IPdR is converted to IUdR.

- IUdR improved clinical outcomes for patients with brain tumors and sarcomas in Phase I/II NIH sponsored clinical trials.

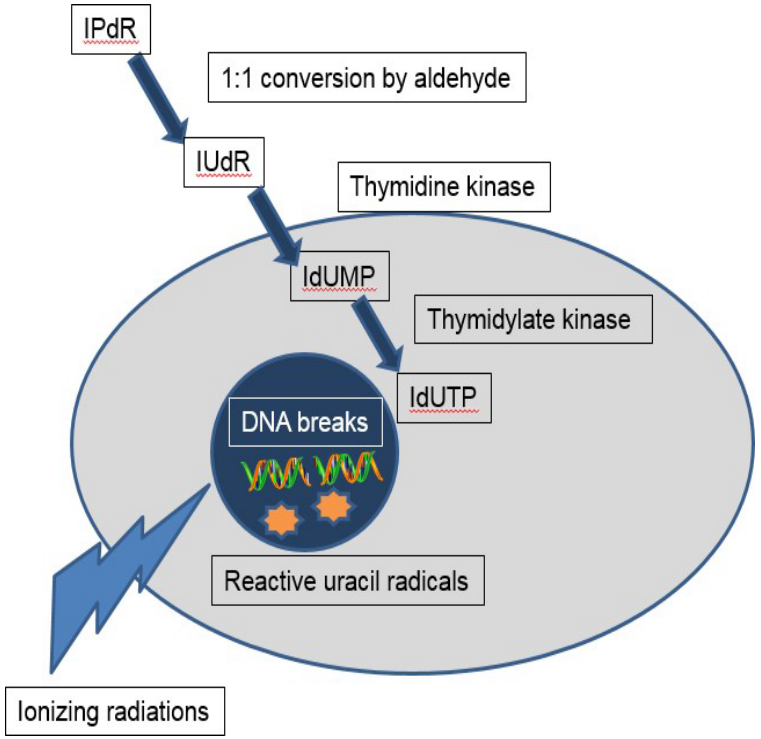


Tumor	Treatment	Median survival (Months)
Anaplastic astrocytomas (Grade 3 of 4)*	RT alone	24
	RT + IUdR	39
Glioblastoma Multiforme (Grade 4 of 4)**	RT alone	9
	RT + IUdR	15

- IUdR requires constant infusion delivery, subject to adverse events.
- IPdR is an orally administered prodrug, converted to IUdR for the sensitizer effect.
- NIH SBIR contract funding was awarded to Shuttle Pharma with a subcontract to Brown University/Rhode Island Hospital to perform the Phase I clinical trial, identifying the MTD.
- Phase I and pharmacology study of Ropidoxuridine and RT (Clin Cancer Res, 2019).
  - 18 patients reached an MTD of Ropidoxuridine with RT of 1200 mg daily for 28 days
  - 14 patients assessed for tumor responses: 4 partial response, 9 stable disease, 1 progressive disease

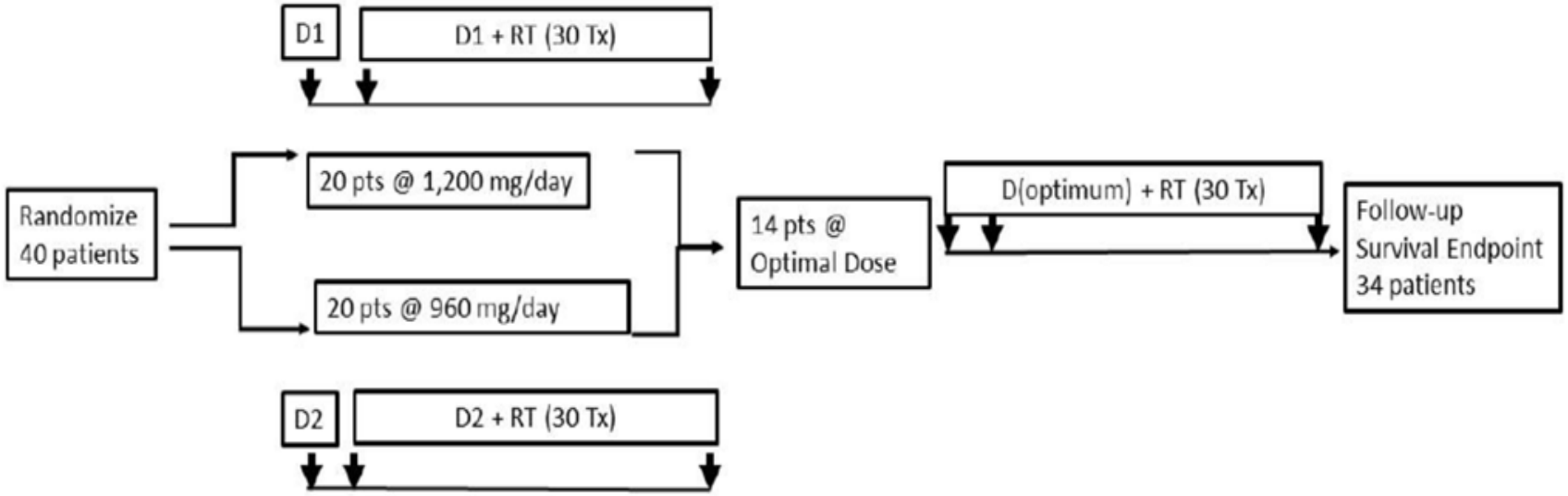
Mechanism

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



Ropidoxuridine (IPdR) – Clinical Asset Development

- **Phase II study of Ropidoxuridine + RT in IDH wild-type, methylation negative glioblastoma patients.**
- **IND has been approved and the FDA has issued a safe to proceed letter.**



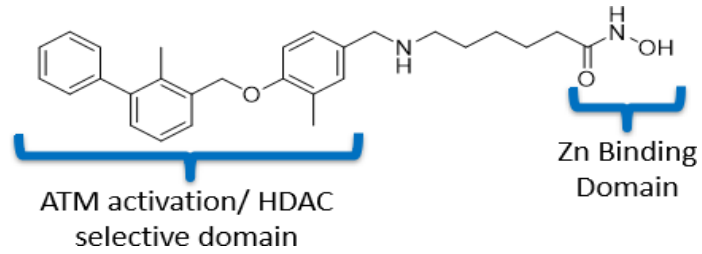
- **TCG GreenChem manufactured API, University of Iowa Pharmaceuticals formulated the drug product (capsules).**
- **Theradex Oncology provides CRO services for the multi-institutional, IRB approved, Phase II clinical trial.**
- **Clinical enrollment will take place at 6 East Coast Cancer Centers. The University of Miami and University of Virginia are first to complete contract negotiations and IRB approvals and are ready to initiate enrollment.**
- **Enrollment is anticipated to require 12 to 18 months. Early results readout is anticipated in ~ 24 months.**

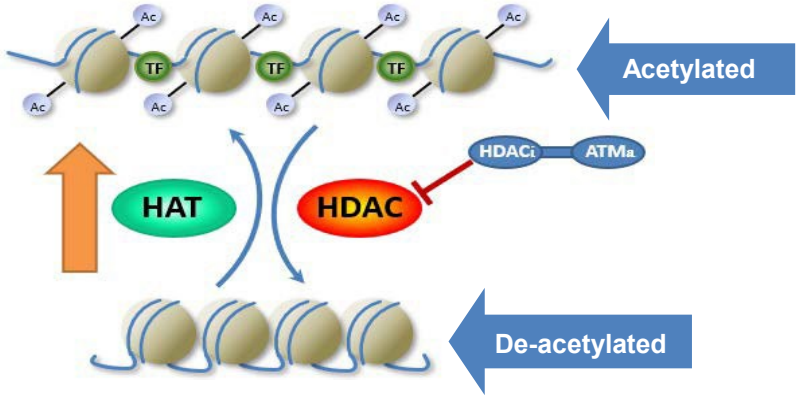
Therapeutics: Development of Selective HDAC Inhibitors

Therapeutic Pipeline includes histone deacetylase inhibitors for post-RT immune stimulation (SP-2-225) and treatment of ER+ breast cancers.

		Pre-clinical	Phase 1	Phase 2	Phase 3	Next Anticipated Milestone
DNA Mediated Radiation Sensitization	Ropidoxuridine – Brain Tumors and Sarcomas					Initiate Phase II Clinical Testing
	IPdR + TPI – Proton Beam					IND Enabling Study
HDAC Inhibitor Platform Technology	Class II HDAC6 Selective		SP-2-225 Activates Post-RT Immune System			IND Enabling for Clinical Testing Multiple Sites
	Class I – ER+ Targeting		SP-1-303 Inhibits ER+ Breast Cancer Growth			IND Enabling for Clinical Testing Breast Cancers
	Dual Function Pan HDAC		SP-1-161 Sensitizes Head & Neck Cancers			IND Enabling Clinical Testing H&N, Lung

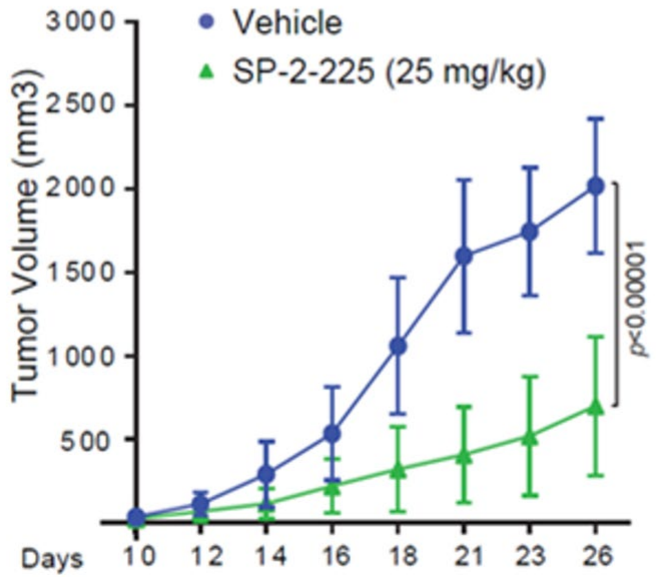
Mechanism
HDAC inhibitors





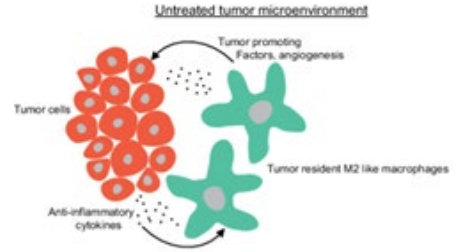
- Shuttle Pharma has discovered novel HDAC inhibitors using proprietary technology.
- SP-2-225 is our candidate lead HDAC6 inhibitor for RT and immunotherapy treatment.
- HDAC6 inhibitor SP-225 testing will define post-RT immune response enhancement for a role in controlling local and metastatic disease.
- SP-1-303 has been selected for development for breast cancer treatment.

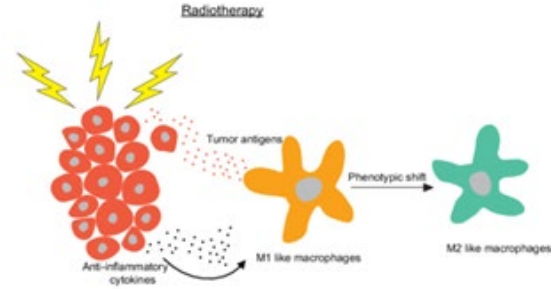
Therapeutics: Selective HDAC6 Inhibition with SP-2-225

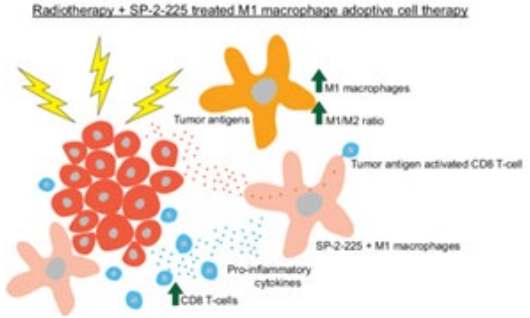


SP-2-225 inhibits HDAC6, prolongs macrophage polarization in M-1 state, resulting in an enhanced inflammatory response to immunogenic cancers and Irradiated tumors.

The next step is to perform IND-enabling studies and perform a Phase I clinical trial







Noonepalle SKR et al, Radiotherapy-induced Immune Response Enhanced by Selective HDAC6 Inhibition. Mol Cancer Ther. 2023 PMID: 37586844; PMCID: PMC10878032.

Therapeutics: Clinical and Pre-clinical Development Strategies

- **Clinical development of Ropidoxuridine & RT**
  - **Perform the Phase II clinical trial of Ropidoxuridine & RT in brain tumors**
  - **Seek FDA "breakthrough" designation and early marketing approval on glioblastoma**
  - **Prepare Ropidoxuridine & RT randomized clinical trial for full marketing approval**
  - **Perform a Phase II clinical trial in patients presenting with sarcomas**

- **Pre-clinical development of HDAC6 selective inhibitor SP-2-225**
  - **Scale-up manufacturing and perform IND-enabling of SP-2-225**
  - **Perform the Phase I clinical trial of SP-2-225 and RT in multiple sites**

- **Pre-clinical development of HDAC 1&3 selective inhibitor SP-1-303**
  - **Scale-up manufacturing and perform IND-enabling of SP-1-303**
  - **Establish academic collaboration to test for pre-clinical, in vivo efficacy**
  - **Perform the Phase I clinical trial of SP-1-303 in advanced breast cancers**
  - **Perform the Phase I clinical trial of SP-1-303 and RT in breast cancers**

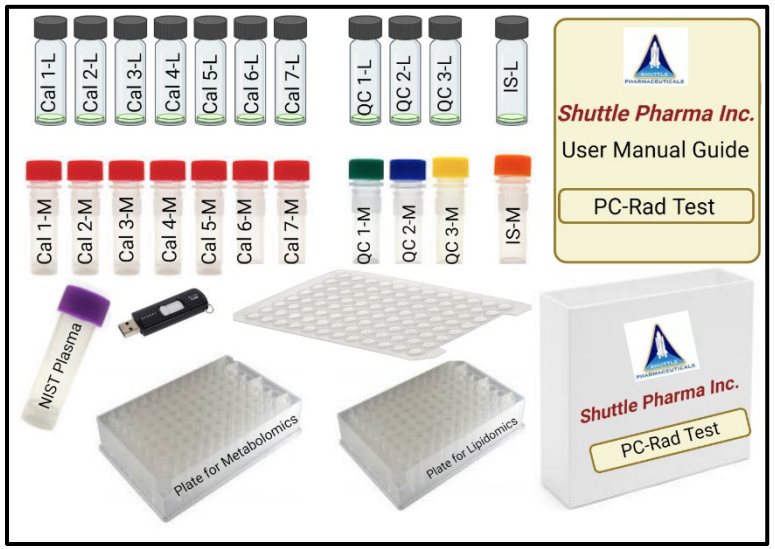
Diagnostics : Clinical Validation of the PC-Rad Test

- **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 for prostate cancer offer prognosis of disease and potential interventions.**
- **In 2019, the estimated global prostate cancer diagnostic market was $2.83 billion.**
- **None of the currently available tests are predictive of success of a specific treatment.**
- **The key unmet need is for a minimally invasive diagnostic test that provides the clinician and patient with a measurement of the potential success of RT for their cancer treatment.**

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**



Source: American Cancer Society Facts & Figures, National Cancer Institute Cancer Statistics 2020
Clarivate Research; Prostate Cancer – Landscape & Forecast – Disease Landscape & Forecast, published January 2023

Theranostics/Diagnostics: Product Development – PSMA-B

The **prostate-specific membrane antigen (PSMA)** is located on the outside of prostate cancer cells.

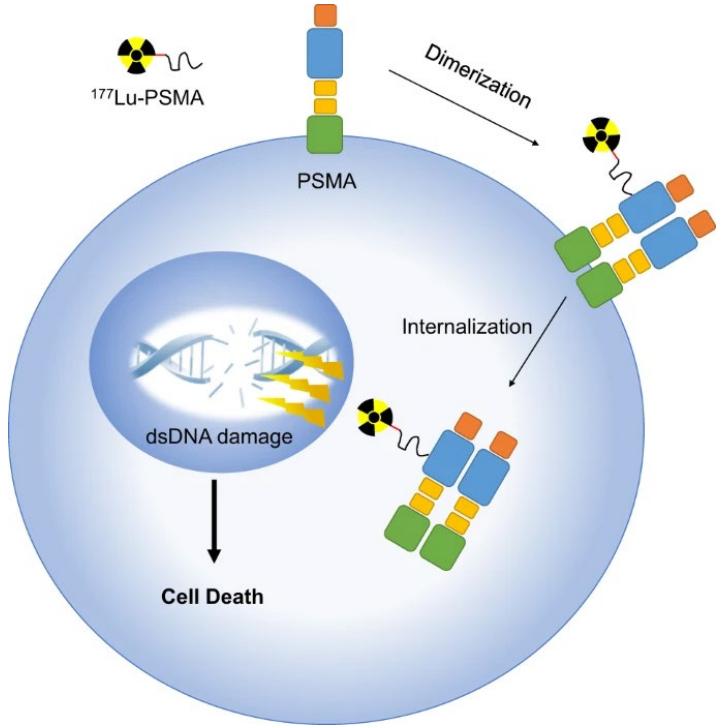
The **PSMA ligand** binds to PSMA, dimerizes, and is internalized into the cell.

Diagnostic molecules for PET scanning are created by attaching radioisotopes (such as F-18 or Gallium-68) to the PSMA ligand for injection into patients to perform PET scans.

Therapeutic molecules are created by attaching other radioisotopes (Lu-177) for administration of therapeutic doses of radiation targeted to PSMA bearing prostate cancer cells.

PSMA-B was designed by Shuttle Pharma scientists for prostate cancer sensitization to particle RT.

PSMA-B is active at nano-molar concentrations and will be evaluated for potential use in diagnostic and therapeutic applications.



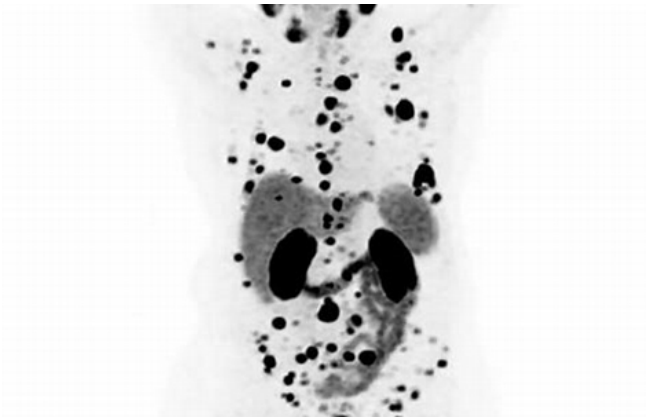
Jia AY, Kiess AP, Li Q, Antonarakis ES. Radiotheranostics in advanced prostate cancer: Current and future directions. Prostate Cancer Prostatic Dis. 2024.. PMID: 37069330.

Theranostics: PSMA-B 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.**
- **Pluvicto (^{177}Lu-PSMA-617), a targeted radiopharmaceutical treatment for PSMA-positive metastatic prostate cancer has a predicted market size of $ 2 billion.**
- **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.**

PET Scan
Widely metastatic prostate cancer



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

Intellectual Property

Ropidoxuridine (radiation sensitizers)

- **Orphan disease designation, method of use patent for next generation IPdR/TPI formulation, manufacturing patents.**

Selective HDAC inhibitors (radiation sensitizers/immune modulators)

- **> 20 composition of matter HDAC inhibitor patents in the U.S., Canada and Europe.**
- **HDAC6 (Class IIb) selective SP-2-225, HDAC 1 and 3 (Class I) selective HDAC selective inhibitor SP-1-303.**
- **Patents are Company property, invented by Shuttle Pharma's scientists requiring no milestone or royalty payments.**

PC-RAD Test (predictive biomarker)

- **Metabolomics-based diagnostic predictive biomarker. Exclusive licensed intellectual property from Georgetown University.**

PSMA-B (theranostic/diagnosis)

- **Boron containing PSMA ligand for use in the treatment and diagnosis of prostate cancer. Exclusively developed for Shuttle Pharma and licensed from inventors.**

Clinical Development Strategy for Shuttle Diagnostics

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

Predictive Biomarker for Prostate Cancer

- Establish and 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 prostate cancer patients receiving RT.

Develop PSMA-B intellectual property for theranostic applications

PSMA-B ligand evaluation for diagnosis and therapy

- PSMA-B cellular studies to determine sensitization to proton and neutron radiation.
- PSMA-B imaging studies in an animal model of prostate cancer (academic collaboration).
- Exploratory studies to synthesize and screen PSMA-B ligand-drug conjugates.

Financial Overview

Shuttle Pharmaceuticals Cap Table as of June 30, 2024	
Common Stock	2,026,838
Fully Vested Restricted Stock Units (RSUs)	79,395
RSUs Outstanding	58,839
Warrants Outstanding	184,000
Total Shares on a Fully Diluted Basis	2,349,072

Capital Market Profile	
Exchange/Ticker	NASDAQ: SHPH
Closing Stock Price*	$1.76
52 Wk High/Low*	$1.28 - $5.76
Market Cap*	$3.8M
Cash Balance (6/30/24) [1]	$2.34M

[1] Including marketable securities

* As of 9/17/2024

Shuttle's Experienced Leadership Team

Anatoly Dritschilo, MD
CEO & Chairman

- Founder & CEO of Shuttle Pharma since 2012; Chairman, Board of Directors 2017
- Former Member, Board of Directors, Neopharm Inc.
- Academic career: Georgetown University School of Medicine, Chairman, Department of Radiation Medicine, Medical Director Georgetown University Hospital, interim Director, Lombardi Cancer Center
- Fellow ACR, NAI

Peter Dritschilo, MBA
President & COO

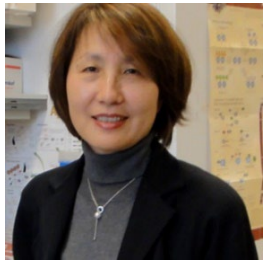
- President & COO of Shuttle Pharma 2012
- CFO Shuttle Pharma 2012-2019
- Co-Founder Shuttle Pharma 2012
- Radiation oncology administrator:
- Rad America, Inova Health
- MBA George Washington University

Michael Vander Hoek , MHSA
CFO and VP Regulatory

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

Tyvin Rich, MD
Medical Director

- Medical Director 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



Mira Jung, PhD
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

Timothy J. Lorber, CPA
CFO

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

Board of Directors

Steve Richards, MBA, CPA

Businessman
CEO, Endurance Media

- Founder and CEO of Endurance Media
- Former Co-President and COO Silver Pictures
- Expertise in financial structuring, capital procurement, strategic business development, corporate management
- MBA, UCLA, Anderson School, CPAF
- Chair, Audit and Corporate Governance Committees

Milton Brown, MD, PhD

Vice Dean for Research
East Virginia Medical School

- Former Professor & Director, Drug Discovery Center, Georgetown University/LCC
- Former Director, Center for Drug Discovery at George Mason University
- Former Director, Inova Center for Drug Discovery and Development
- Co-Founder Shuttle Pharma 2012
- PhD Chemistry, University of Alabama
- MD University of Virginia

Bette Jacobs, PhD

Professor/Distinguished Scholar
Georgetown University

- Distinguished Scholar and co-founder at the O'Neill Institute for National and Global Health Law
- Fellow and Visiting Professor at Campion Hall University of Oxford
- Former Dean, Georgetown University School of Nursing and Health Studies
- Former Vice President for Honda of America Manufacturing

Chris Senanayake, PhD

CEO, TCG GreenChem

- Founder and Chief Executive Officer (CEO) of TCG GreenChem Inc.
- Chief Scientific Officer of TCG Lifesciences
- Former Senior Scientist at Dow Chemical
- Former Vice President of Chemical Development for Boehringer Ingelheim Pharmaceuticals

Joshua Schafer, MBA

Chief Commercial Officer
& EVP of Business Development
Zevra Therapeutics

- Former VP, Business Development & Strategy, Mallinckrodt Pharmaceuticals
- Former VP, Astellas Pharma
- Director Oncology Marketing of Takeda Pharma
- MBA, Northwestern University, Kellogg School
- Chair Compensation Committeel

THANK YOU

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