Shuttle Pharmaceuticals Holdings, Inc.

Nasdaq: SHPH

Investor Presentation

Fall 2024

Forward Looking Statements

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Anatoly Dritschilo, MD, FACR
CEO, Shuttle Pharmaceuticals Holdings, Inc.
401 Professional Drive, Suite 260
Gaithersburg, MD 20879
Phone: 240-403-4212
anatoly.dritschilo@shuttlepharma.org

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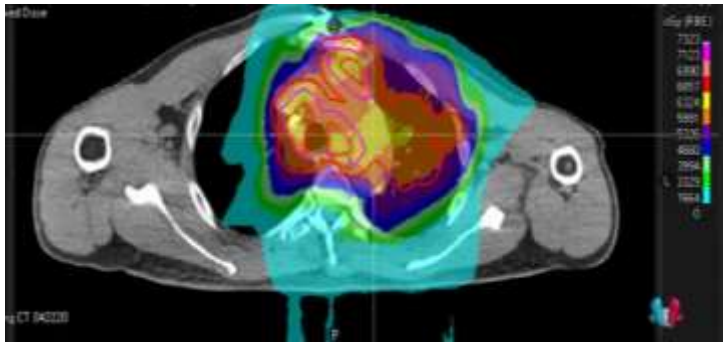
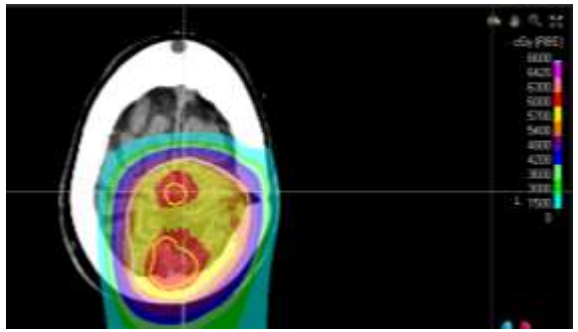
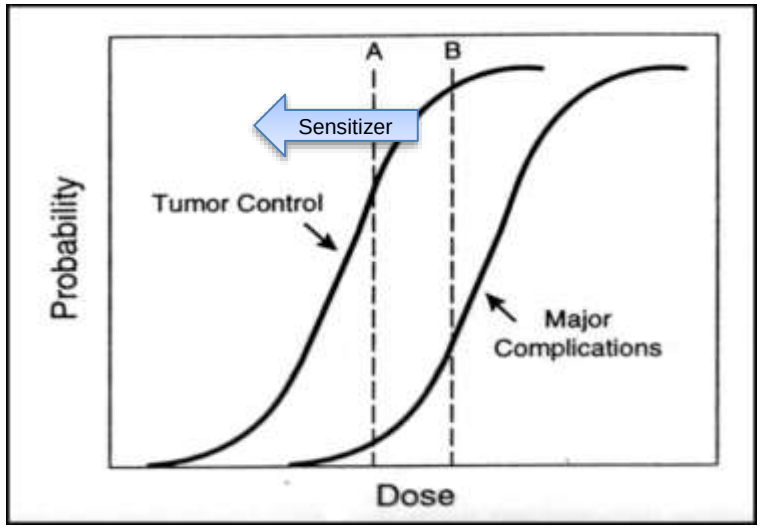
The Fundamental Problem of Radiation Therapy:

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







Sensitization of cancer cells to radiation therapy

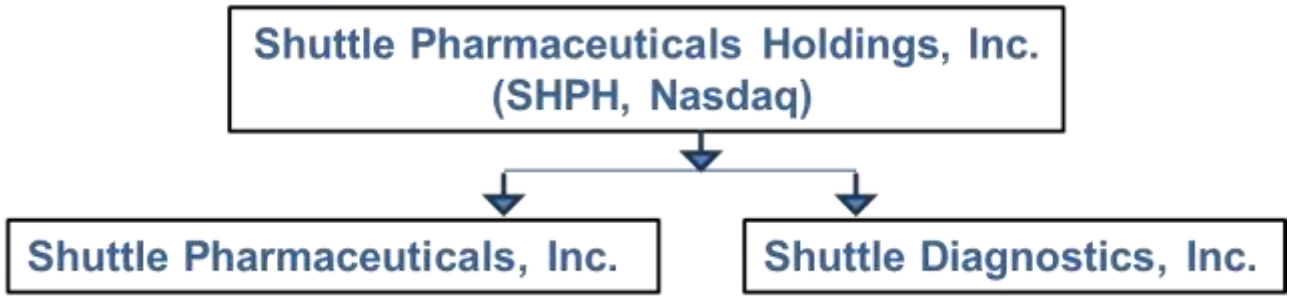
- Radiation dose determines cancer curability
- Radiation therapy limitations are due to sensitive adjacent normal tissues
- Sensitizer drugs make cancer cells more sensitive to radiation therapy
- Currently available sensitizer drugs are mostly used “off-label”

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
- HDAC6 selective inhibitors enhance immune responses in pre-clinical models

Company Overview: drugs combined with RT for cancer treatment

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

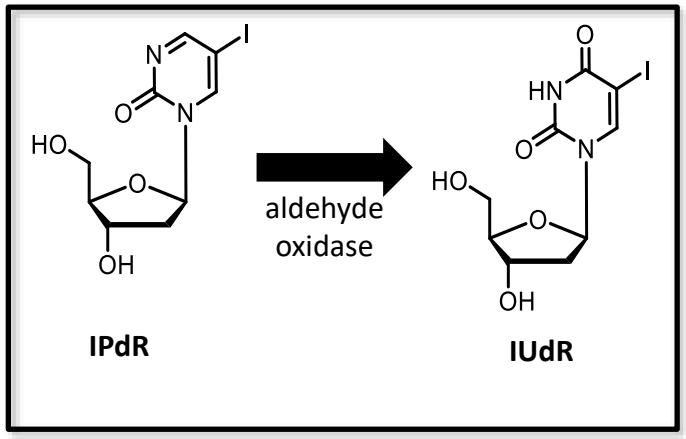
- **Ropidoxuridine** is a clinical stage, orally-administered cancer radiation sensitizer
- **SP-2-225** is a pre-clinical stage, selective HDAC6 inhibitor for innate post-RT immune system activation

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?

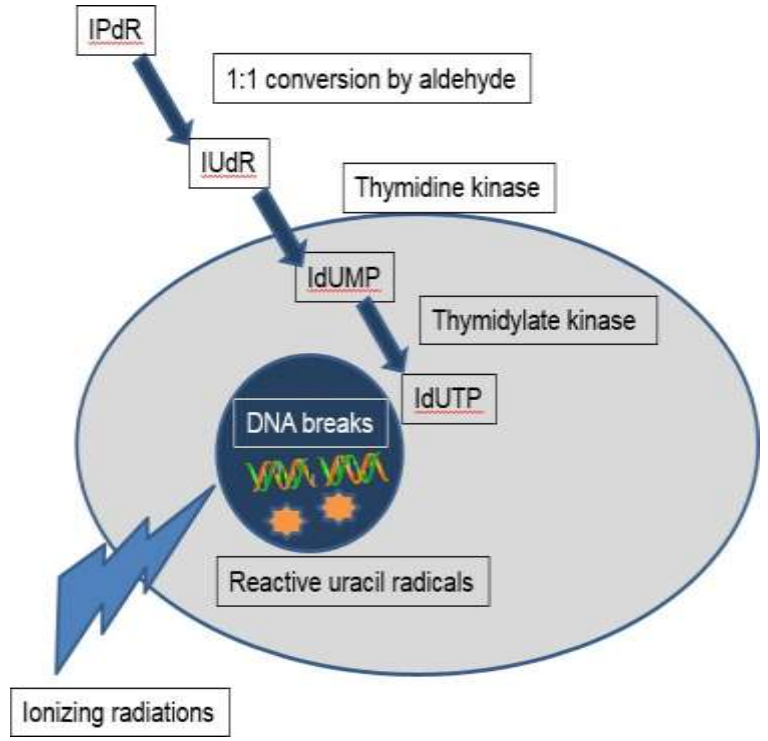
Ropidoxuridine (IPdR) is the prodrug of IUdR, a powerful radiation sensitizer, reported to improve clinical outcomes of patients treated for brain tumors and sarcomas in NIH supported Phase I/II clinical studies.



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.

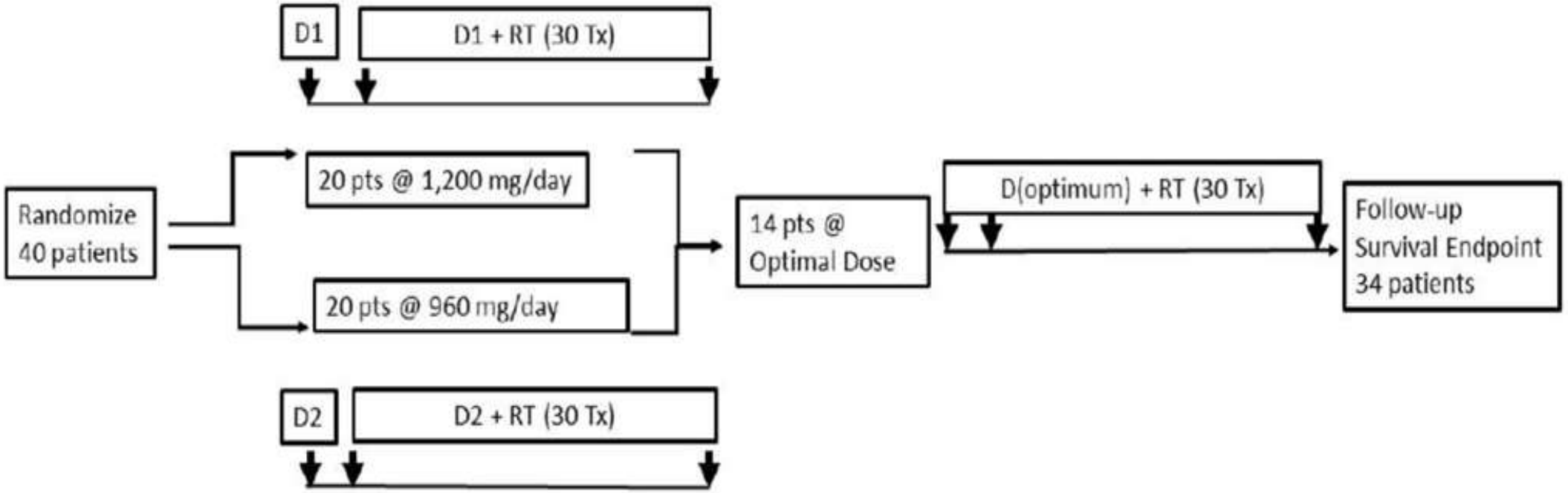


Comments and Observations

- **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) – Clinical Asset Development

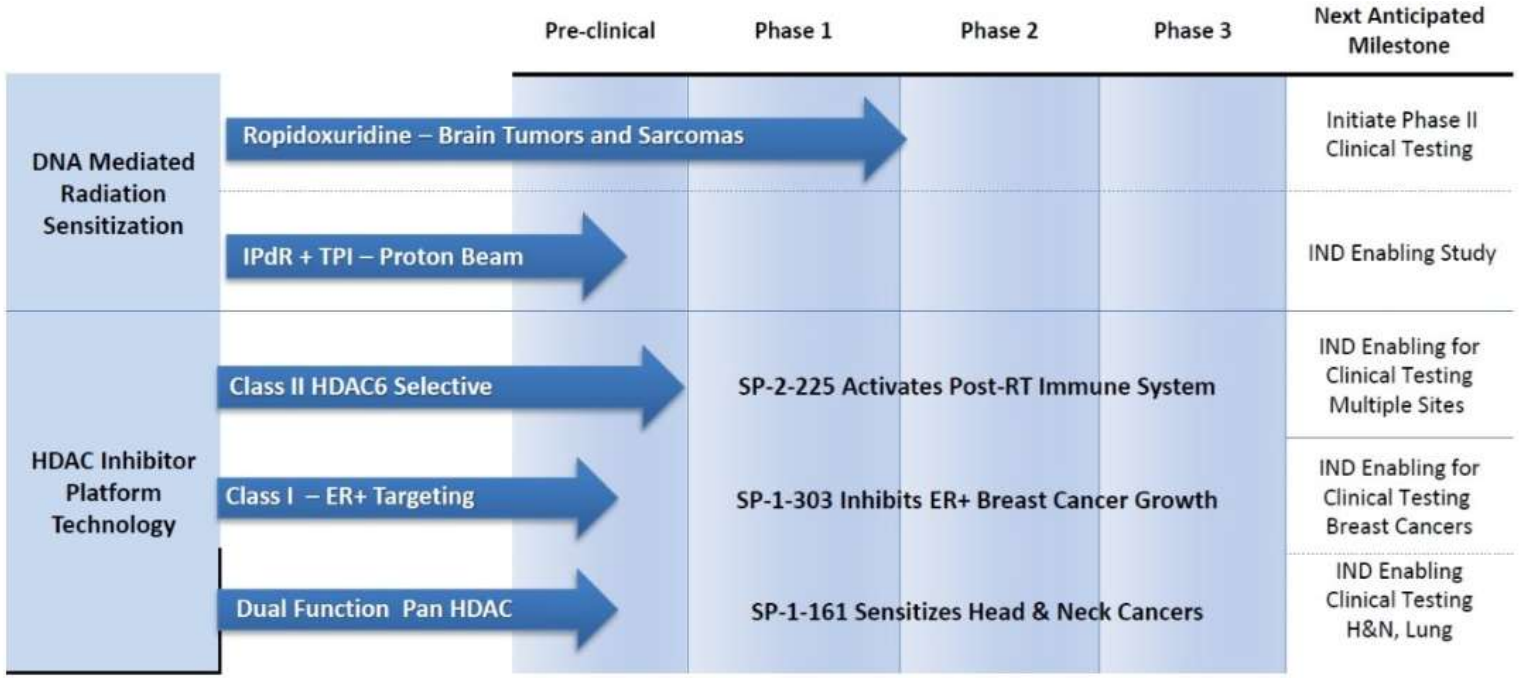
- **Phase II study of Ropidoxuridine + RT in IDH wild-type, methylation negative glioblastoma patients.**



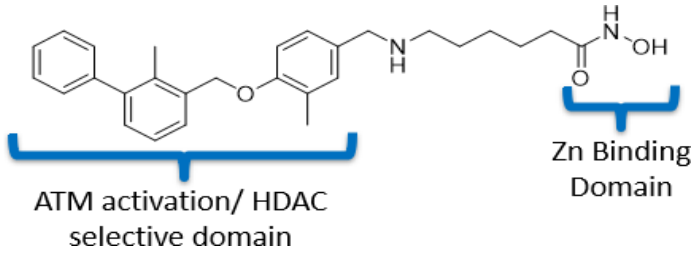
- **TCG GreenChem manufactured API, University of Iowa Pharmaceuticals formulated the drug product (capsules).**
- **Theradex Oncology provides CRO services for the multi-institutional, IRB approved, Phase II clinical trial.**
- **IND has been approved and the FDA has issued a safe to proceed letter.**
- **Clinical enrollment has been initiated. Six (6) East Coast Cancer Centers have been engaged.**
- **Enrollment is anticipated to require 12 to 18 months. Early results readout is anticipated in ~ 24 months.**

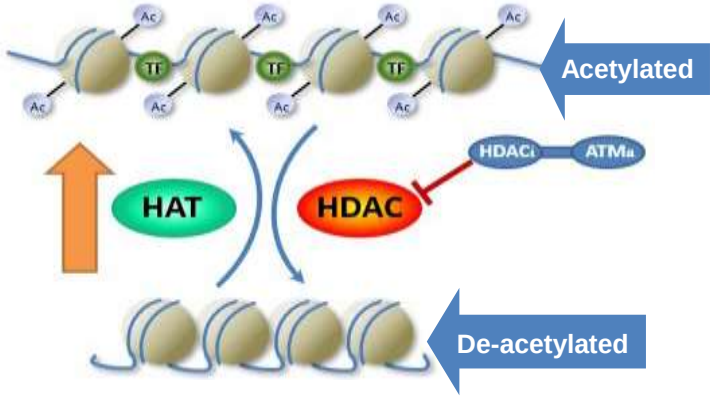
Therapeutics: Selective HDAC Inhibitor Development

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



Mechanism
HDAC inhibitors

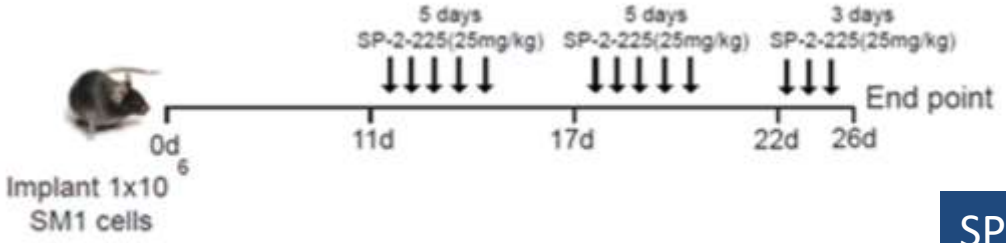


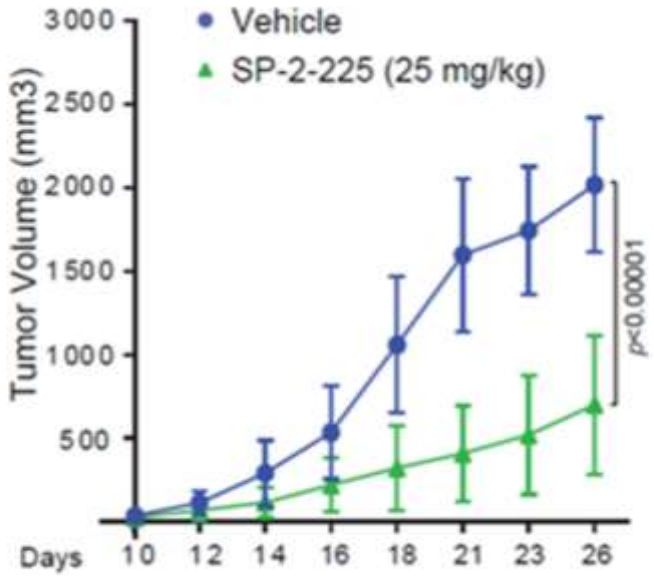


Comments and Observations

- **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.**

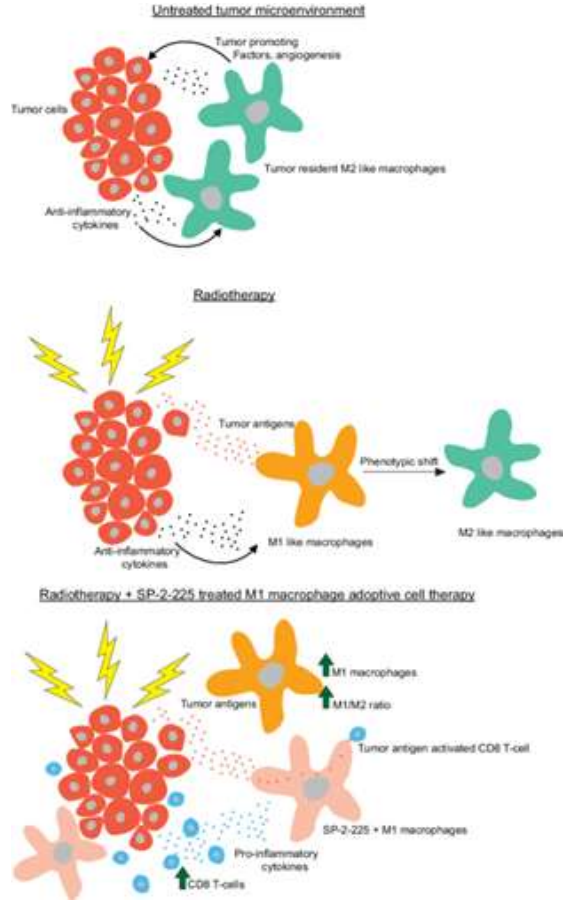
Therapeutics: HDAC6 selective inhibition with SP-2-225





SP-2-225 inhibits HDAC6, prolongs macrophage polarization in the M-1 (inflammatory state), resulting in an enhanced immunogenic response to cancer antigens 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

1. **Clinical development of Ropidoxuridine & RT**
    - **Complete the Phase II clinical trial of Ropidoxuridine & RT in glioblastoma brain tumors**
    - **Seek FDA "breakthrough" designation and early marketing approval for glioblastoma indication**
    - **Prepare Ropidoxuridine and RT randomized Phase III clinical trial for full marketing approval**
    - **Perform a Phase II clinical trials to expand clinical indications to sarcomas**

2. **Pre-clinical development of HDAC6 selective inhibitor SP-2-225**
    - **Scale-up manufacturing and formulation**
    - **Perform IND-enabling studies of SP-2-225 for a Phase I clinical trial**
    - **Perform the Phase 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**
    - **Contract academic institution to test pre-clinical, in vivo efficacy, in ER+ beast cancer models**
    - **Perform IND-enabling studies of SP-1-303 for a Phase I clinical trial**
    - **Perform the Phase I clinical trial of SP-1-303 in advanced breast cancers**

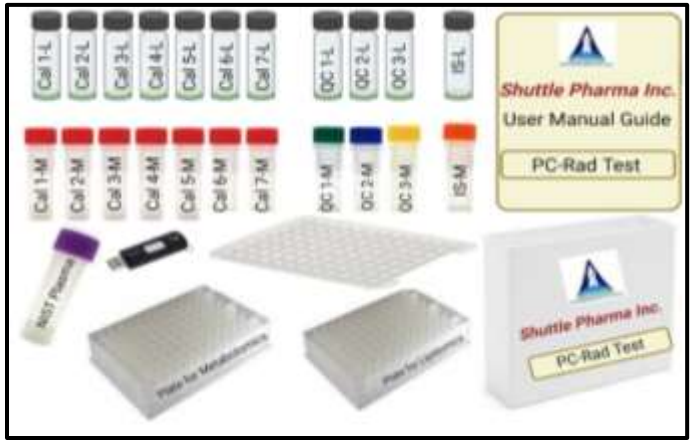
Diagnostics: Clinical Validation of the PC-Rad Test

- **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.**

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**

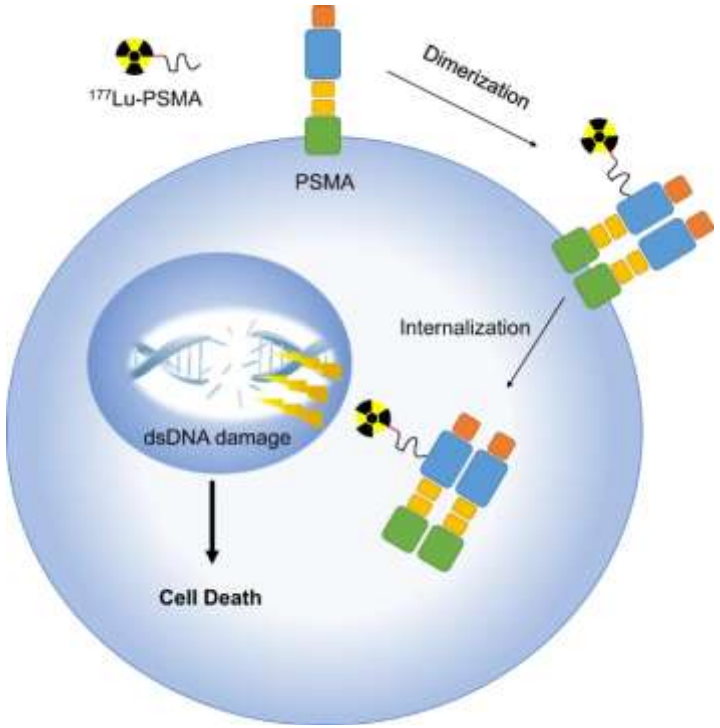


Sources: American Cancer Society Facts & Figures, National Cancer Institute Cancer Statistics 2020
Clarivate Research; Prostate Cancer – Landscape & Forecast – Disease Landscape & Forecast, published January 2023
Grandview Research – Market Analysis Report - 2023

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

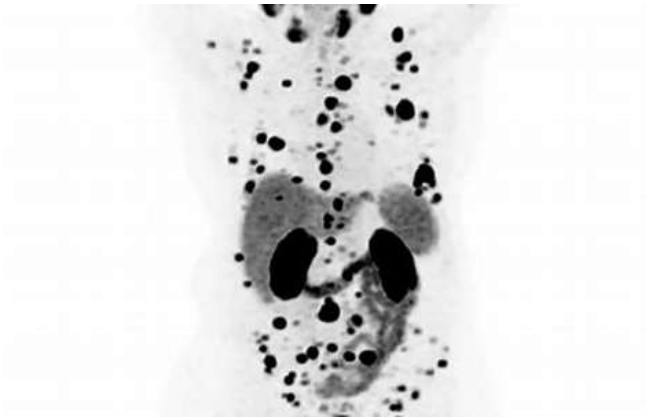
Market Opportunity: PSMA imaging and therapy

- **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

- 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 as primary treatment for localized disease.

2. Develop PSMA-B intellectual property for theranostic applications

PSMA-B ligand evaluation for diagnosis and therapy

- Complete PSMA-B cellular studies to determine sensitization to proton and neutron radiation.
- Perform radioisotope labelled PSMA-B imaging studies in an animal model of prostate cancer (academic collaboration).
- Synthesize and screen PSMA-B ligand-drug conjugates for targeted prostate cancer treatment.

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.**
- **Patents are the Company's exclusive properties, invented or co-invented by Shuttle Pharma's scientists, no milestones or royalty payments.**

3. PC-RAD Test (predictive biomarker)

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

4. PSMA-B (theranostic/diagnosis)

- **Boron containing PSMA ligand for use in the treatment and diagnosis of prostate cancer. Exclusively developed for Shuttle Pharma by collaboration with non-company chemists and exclusive license of intellectual property from inventors.**

Financial Overview

Shuttle Pharmaceuticals Cap Table as of September 30, 2024	
Common Stock	2,946,099
RSUs Outstanding	53,838
Warrants Outstanding	184,000
Total Shares on a Fully Diluted Basis	3,183,937

Capital Market Profile	
Exchange/Ticker	NASDAQ: SHPH
Closing Stock Price*	$1.34
52 Wk High/Low*	$1.03 - $4.94
Market Cap*	$3.9M

* As of 10/23/2024

Experienced Leadership Team

Anatoly Dritschilo, MD
CEO & Chairman

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

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

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 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

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
- 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

Shuttle Pharmaceuticals Holdings, Inc.
Anatoly Dritschilo, MD, CEO
Tel: (240) 403-1212
Email: anatoly.dritschilo@ShuttlePharma.org

Investor Relations
Lytham Partners
Robert Blum
Tel: (602) 889-9700
Email: SHPH@LythamPartners.com