Shuttle Pharmaceuticals Holdings, Inc.

Nasdaq: SHPH

Investor Presentation
February 2024

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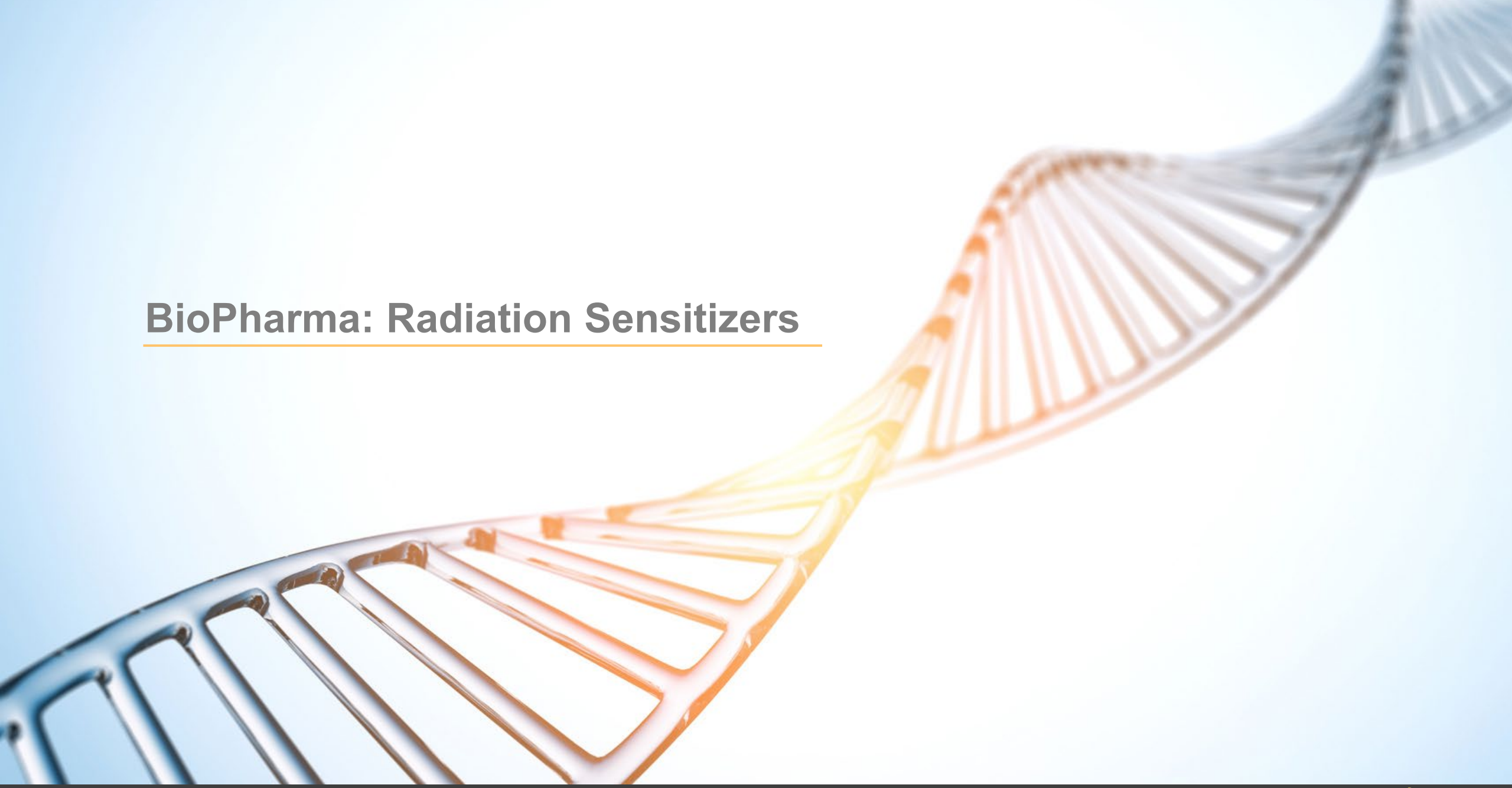
Company Overview

Shuttle Pharma (Nasdaq: SHPH) is a clinical-stage biopharma company developing next generation drugs and diagnostics designed to improve radiation therapy outcomes.

- **Biopharma Therapeutics**
  - **Mission is to improve the lives of cancer patients receiving Radiation Therapy (RT) by increasing cure rates and decreasing toxicities.**
    - Radiation sensitizers can increase cancer cure rates, prolong patient survival and improve quality of life.
    - Immunity activators (SP-2-225) can improve radiation therapy outcomes by stimulating the immune responses to irradiated cancers.
  - **Ropidoxuridine, the Company's lead candidate, is an orally available prodrug that, once ingested, metabolizes into iododeoxyuridine (IUdR), a pyrimidine analog that has been recognized since the 1960s as a potent radiation sensitizing agent.**
    - Clinical advancement includes successful completion of the Phase I clinical trial of Ropidoxuridine and RT and FDA approval of the IND to perform the Phase II trial in brain cancer patients presenting with glioblastoma.
    - Ropidoxuridine and RT pipeline potentially includes brain tumors, sarcomas, lung and GI cancers.
    - Currently, there is only one marketed drug specifically approved for radiation sensitization; the other sensitizers are chemotherapeutics used "off label" by oncologists with radiation sensitization as a secondary drug property.
  - **Selective HDAC6 inhibition by SP-2-225, a pre-clinical stage molecule, activates the innate immune system to target irradiated tumor cells by immune mechanisms.**
    - Pre-clinical studies of HDAC inhibitors have potential indications for treating multiple myeloma, breast cancer, lung cancer and malignant melanoma.
- **Diagnostics**
  - **Strategic focus is on developing pretreatment predictive blood tests for prostate cancer patients who are considering elective radiation therapy to allow risk assessment for treatment success or failure, to inform therapeutic decisions and follow-up management.**

BioPharma: Radiation Sensitizers



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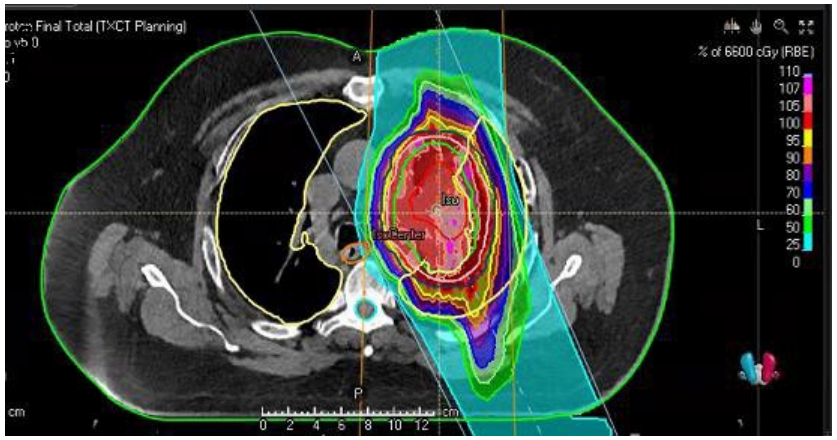
The Fundamental Problem Facing Radiation Therapy

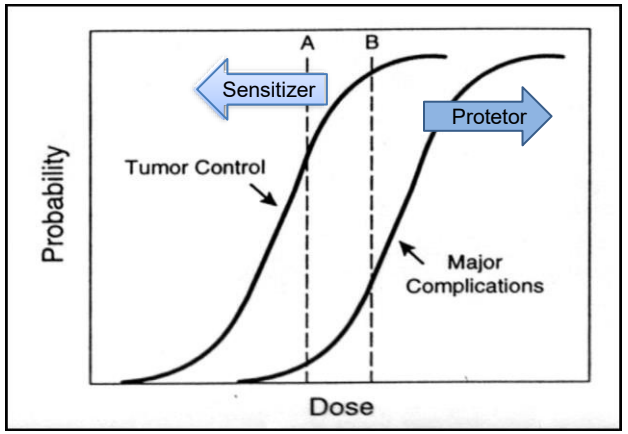
Cancers are resistant to cure by radiation therapy because tumors are surrounded by radiation sensitive normal tissues that limit the maximum treatment dose

Strategies to overcome cancer resistance to radiation therapy:

- **Sensitize Cancer Cells To Radiation Therapy**
  - Radiation sensitizers improve cancer control at tolerable doses in cancers of the lung, GYN and GI
  - Shuttle Pharma believes our Ropidoxuridine platform technology addresses this unmet clinical need

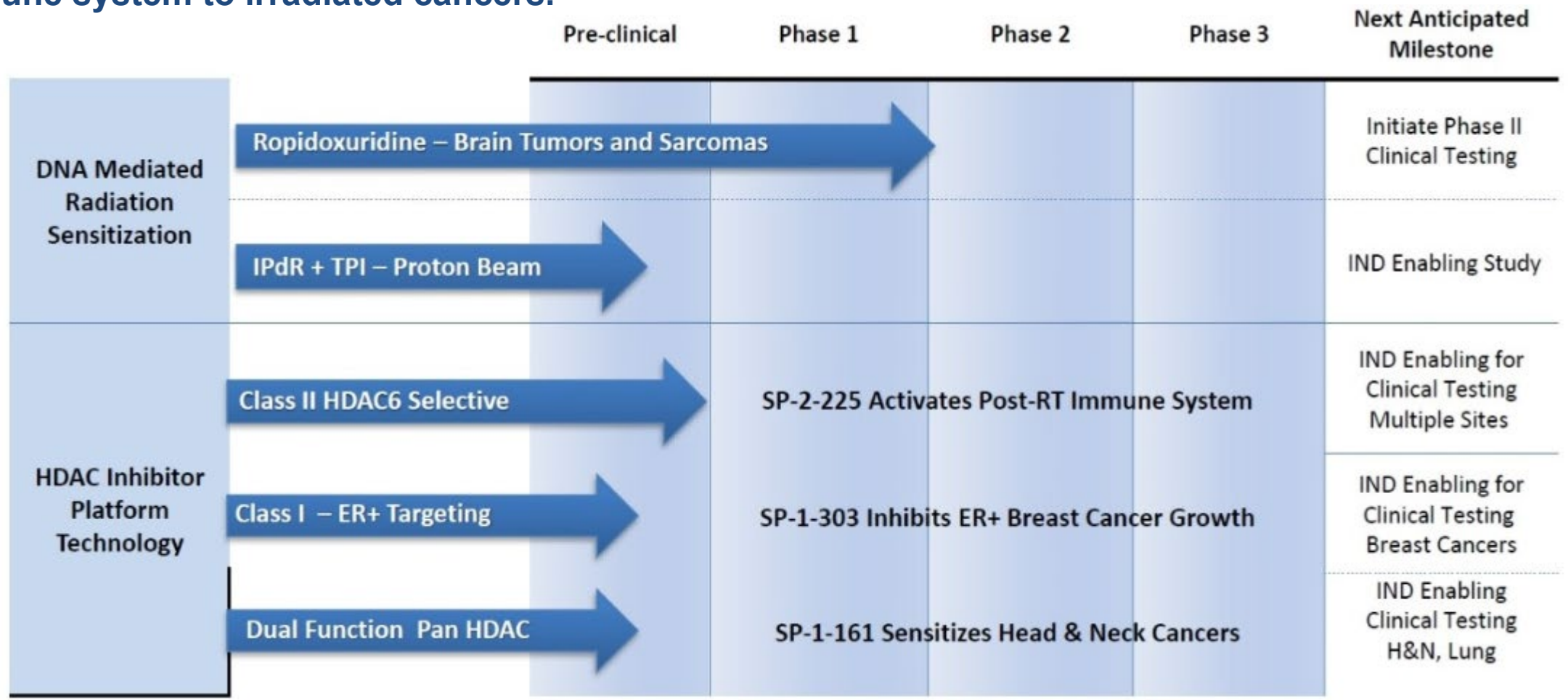
- **Activate The Immune Response To Irradiated Cancers**
  - Irradiated cancer cells express cellular antigens that activate the immune system
  - Shuttle Pharma's HDAC6 selective inhibitor SP-2-225 is designed to enhance the immune response to inhibit tumor growth





Radiation Sensitizers: Pipeline

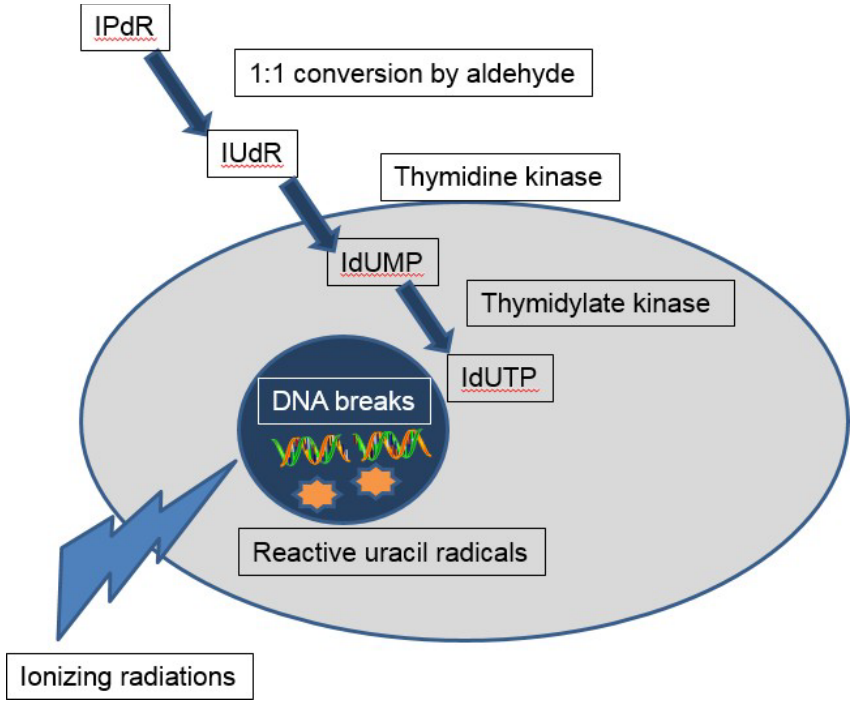
Pipeline composed of two parts: Ropidoxuridine is the lead clinical drug candidate for sensitizing rapidly growing cancer cells and, selective HDAC (histone deacetylase) inhibitors which stimulate the immune system to irradiated cancers.



Ropidoxuridine Platform: Clinical Studies

- **Ropidoxuridine (IPdR) is the prodrug of IUdR**
  - IUdR is a powerful radiation sensitizer showing Phase II efficacy in NIH sponsored clinical trials
    - IUdR and RT improved survival for glioblastoma and anaplastic astrocytoma patients and for sarcoma patients
  - IUdR requires intra-venous, constant infusion delivery subject to drug delivery-related adverse events
  - IPdR is a prodrug, administered orally, and converted to IUdR for sensitizer effect

- **Phase I and pharmacology study of Ropidoxuridine (IPdR) as prodrug for iododeoxyuridine-mediated tumor radiosensitization in advanced GI cancers undergoing radiation (Clin Cancer Res, 2019)**
  - NIH SBIR contract funding was awarded to Shuttle Pharma with subcontract to Brown University/Rhode Island Hospital to perform this study



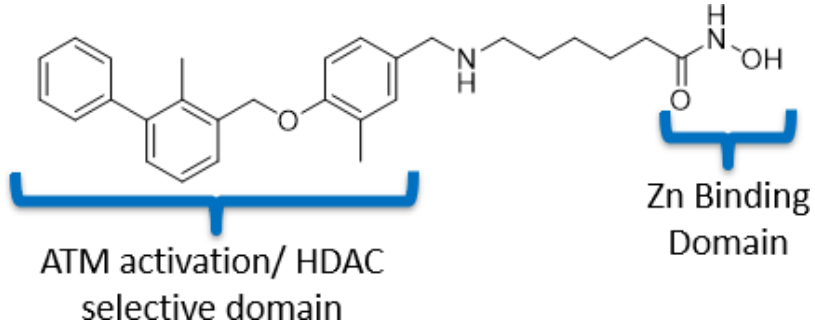
- Oral delivery of IPdR (Ropidoxuridine) with RT is safe and IUdR is bioavailable for cancer sensitization
  - 18 patients reached an MTD of Ropidoxuridine with RT of 1200 mg daily for 28 days
  - 14 patients were assessed for tumor responses: 4 partial responses, 9 stable disease, 1 progressive disease

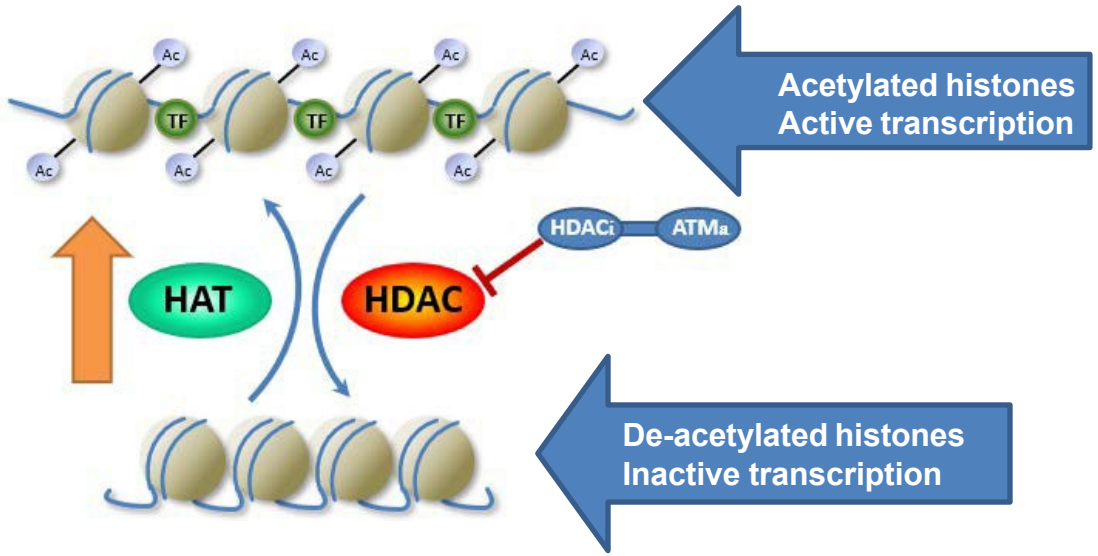
Recent Activities

- **Results of Pre-IND Meeting with the FDA – IND approved, safe to proceed letter received January 5, 2024**
  - The FDA's positive feedback and guidance on the Company's Chemistry, Manufacturing, and Controls (CMC) and clinical protocol design for Ropidoxuridine provided a pathway for IND application submission in the fourth quarter of 2023 to initiate the Phase 2 clinical trial.
  - Engagement of clinical cancer centers for Phase II patient enrollment is in progress.
- **Drug Manufacturing – Drug API has been manufactured and formulated into drug product capsules**
  - Successfully completed the manufacturing campaign for the active pharmaceutical ingredient (API) of Ropidoxuridine for use in Shuttle Pharma's upcoming Phase II clinical trial.
  - Successfully completed the formulation and encapsulation of the Ropidoxuridine drug product for use in Shuttle Pharma's upcoming Phase II clinical trial. Drug is stored with Theradex, the CRO, for distribution for the clinical trial.
- **Intellectual Property Strengthened – Orphan Designation for glioblastoma and next generation patent**
  - U.S. patent # 11,654,157 was awarded for Ropidoxuridine/Tipiracil method of use and therapeutic composition.
- **Laboratory Expansion – New facilities for processing clinical trial-related specimens and tissue culture**
  - Moved into expanded laboratory facilities and office space to enable further development of Shuttle Pharma's lead drug candidates and to accelerate broader diagnostic capabilities on predictive biomarkers of cancer response to treatment.

HDAC Inhibitor Platform: Overview

- Shuttle Pharma has discovered novel HDAC inhibitors using proprietary technology. Cancer radiation sensitization, normal tissue protection and selective HDAC6 inhibition have been observed in preclinical model testing.
- Our HDAC inhibitors are undergoing pre-clinical evaluations of radiation sensitization of solid tumors and activation of the immune response after tumor irradiation.
- SP-2-225 has been selected as our candidate lead HDAC6 inhibitor.
- HDAC6 is a member of the Class IIb HDAC family. Selective HDAC6 inhibitors are an emerging class of pharmaceuticals targeting cancers, neurodegenerative diseases, and immunology.
- The potential to affect regulation of the immune system and enhance the immune response to cancers offers an adjuvant treatment strategy in combination with radiation therapy.
- HDAC6 inhibitor SP-225 testing will define post-RT immune response enhancement for a role in controlling local and metastatic disease.





Intellectual Property Portfolio for Radiation Sensitizers

- **Intellectual property for Ropidoxuridine includes a novel formulation demonstrating improved drug bioavailability**
- **Our HDAC inhibitor intellectual property includes new patent applications and granted patents discovered/invented by Shuttle Pharma scientists.**

Title	Country Name	Patent Number	Status	Issue Date
DUAL FUNCTION MOLECULES FOR HISTONE DEACETYLASE INHIBITION AND ATAXIA TELANGIECTASIA MUTATED ACTIVATION AND METHODS OF USE THEREOF	**United States**	**9,809,539**	**Granted**	**07-Nov-2017**
DUAL FUNCTION MOLECULES FOR HISTONE DEACETYLASE INHIBITION	United States	10,730,834	Granted	04-Aug-2020
DUAL FUNCTION MOLECULES FOR HISTONE DEACETYLASE INHIBITION	United States	10,745,352	Granted	18-Aug-2020
DUAL FUNCTION MOLECULES FOR HISTONE DEACETYLASE INHIBITION	Canada	2,977,996	Granted	22-Aug-2023
DUAL FUNCTION MOLECULES FOR HISTONE DEACETYLASE INHIBITION AND ATAXIA TELANGIECTASIA MUTATED ACTIVATION AND METHODS OF USE THEREOF	**European Patent Convention**	**3265073**	**Granted**	**18-Aug-2021**
DUAL FUNCTION MOLECULES FOR HISTONE DEACETYLASE INHIBITION	France	3265073	Granted	18-Aug-2021
DUAL FUNCTION MOLECULES FOR HISTONE DEACETYLASE INHIBITION	Germany	60 2016 062 395.1	Granted	18-Aug-2021
DUAL FUNCTION MOLECULES FOR HISTONE DEACETYLASE INHIBITION	Hong Kong	HK1250474	Granted	14-Apr-2022
DUAL FUNCTION MOLECULES FOR HISTONE DEACETYLASE INHIBITION	Italy	3265073	Granted	18-Aug-2021
DUAL FUNCTION MOLECULES FOR HISTONE DEACETYLASE INHIBITION	Spain	3265073	Granted	18-Aug-2021
DUAL FUNCTION MOLECULES FOR HISTONE DEACETYLASE INHIBITION	United Kingdom	3265073	Granted	18-Aug-2021
METHODS AND COMPOSITIONS FOR CANCER THERAPIES THAT INCLUDE DELIVERY OF HALOGENATED THYMIDINES AND THYMIDINE PHOSPHORYLASE INHIBITORS IN COMBINATION WITH RADIATION	**United States**	**11,654,157**	**Granted**	**23-May-2023**
SELECTIVE HISTONE DEACETYLASE INHIBITORS FOR THE TREATMENT OF HUMAN DISEASE	**European Patent Convention**	**3565549**	**Granted**	**09-Mar-2022**
SELECTIVE HISTONE DEACETYLASE INHIBITORS	France	3565549	Granted	09-Mar-2022
SELECTIVE HISTONE DEACETYLASE INHIBITORS	Germany	60 2018 031 982.4	Granted	09-Mar-2022
SELECTIVE HISTONE DEACETYLASE INHIBITORS	Hong Kong	40017061	Granted	16-Sep-2022
SELECTIVE HISTONE DEACETYLASE INHIBITORS	Italy	502022000036353	Granted	09-Mar-2022
SELECTIVE HISTONE DEACETYLASE INHIBITORS	Spain	3565549	Granted	09-Mar-2022
SELECTIVE HISTONE DEACETYLASE INHIBITORS	United Kingdom	3565549	Granted	09-Mar-2022
SELECTIVE HISTONE DEACETYLASE INHIBITORS	United States	11,034,667	Granted	15-Jun-2021
SELECTIVE HISTONE DEACETYLASE INHIBITORS	United States	11,584,733	Granted	21-Feb-2023
SELECTIVE HISTONE DEACETYLASE INHIBITORS	United States	11,407,723	Granted	09-Aug-2022

Clinical Development Strategy for Radiation Sensitizers

- **Shuttle Pharma has a broad pipeline to improve clinical outcomes of patients treated with radiation therapy for cancer**

- **Priority #1: Clinical development of Ropidoxuridine & RT**
  - Capitalize on Ropidoxuridine as an orally available, small molecule radiation sensitizer for brain tumors (glioblastoma)
  - Advance FDA “orphan” designation strategy for IPdR in glioblastoma and in sarcomas
  - Next Steps
    - Perform the Phase II clinical trial of Ropidoxuridine & RT in brain tumors
    - Seek FDA “breakthrough” designation and early marketing approval
    - Prepare Ropidoxuridine & RT randomized clinical trial for full marketing approval in glioblastoma treatment

- **Priority #2: Pre-clinical development of HDAC6 selective inhibitor SP-2-225 for immune activation against cancers after RT**
  - Invest in HDAC platform technology development to maximize its utility across cancer therapies.
  - HDAC inhibitor patents (a platform technology) have been granted to Shuttle Pharma
  - Next Steps
    - Perform IND-enabling studies of SP-2-225, manufacture drug product and obtain IND
    - Perform Phase I clinical trial of SP-2-225 administered post RT in patients with advanced cancers

Diagnostics: Predictive Biomarkers

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Diagnostics: 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

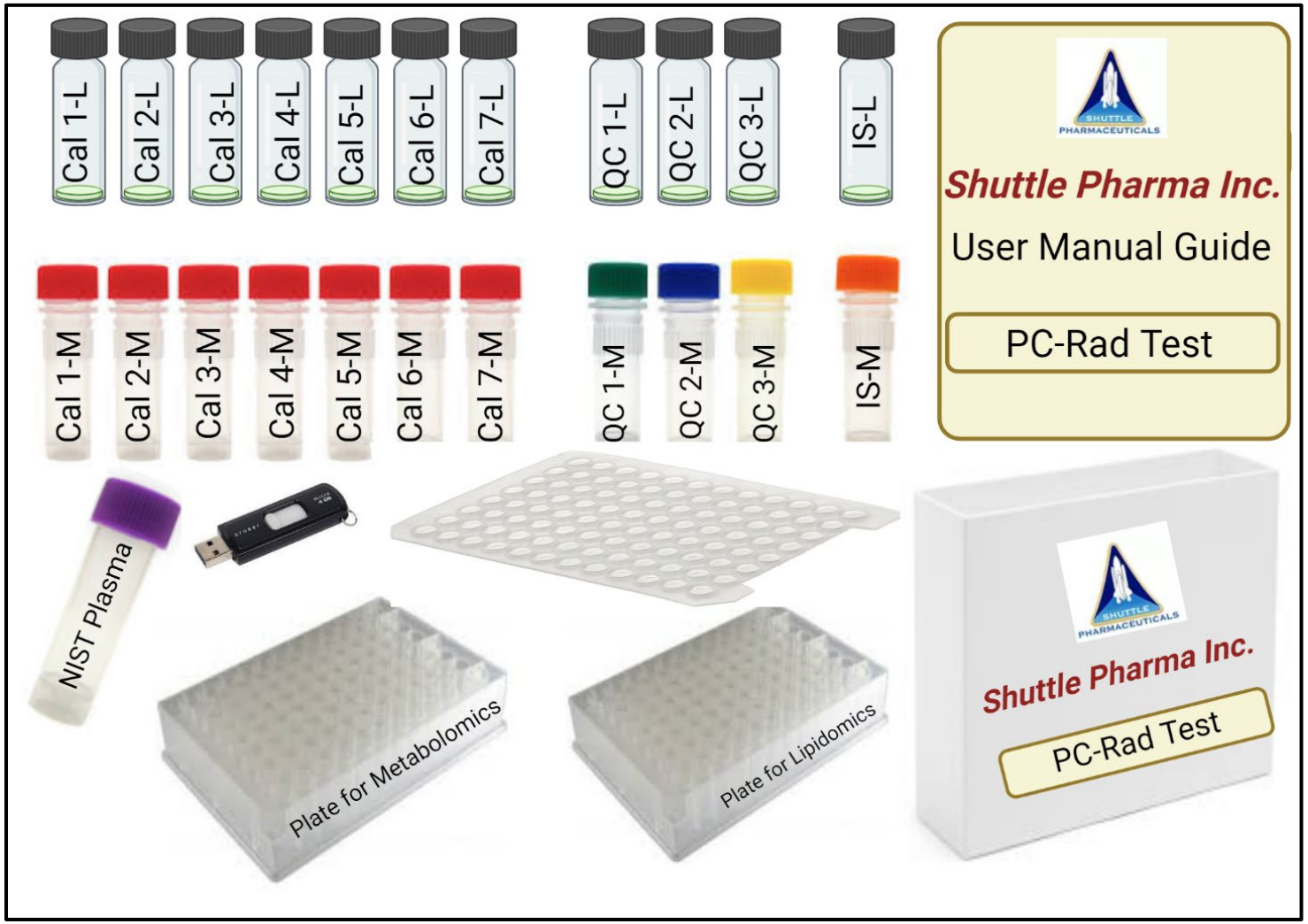
- **Diagnostic tests for prostate cancer offer prognosis of disease and potential interventions.**
- **In 2019, the estimated global prostate cancer diagnostic market was $2.83 billion.**
- **None of the currently available tests are predictive of success of a specific treatment.**
- **The key unmet 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.**

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

Diagnostics: Competitive Landscape

Product category	Method	Main Target	Predictor	Estimated Price
PSA test	Blood	PSA level	Initial diagnosis	$70-$300 per test-various manufacturers
PSMA Scan	Radiopharmaceutical/PET/CT scan	Spread of PCa	Prognosis of disease spread	$1200-$5000
Prolaris®	Tissue biopsy	Genomic mutations	Aggressiveness of PCa cancer	$3800
Decipher®	Tissue biopsy	Genomic mutations	Aggressiveness of PCa cancer	$5000
Oncotype DX®	Tissue biopsy	Genomic mutations	Aggressiveness of PCa cancer	$4200
4Kscore	Blood	Protein measurement using algorithm	Aggressiveness of PCa cancer	$600
Prostate Health Index	Blood	tPSA,fPSA, proPSA	Need for biopsy	$130-$300-various manufacturers

Diagnostics: Product Development



- 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: Clinical Development

1. Establish and validate the predictive assay by performing a muti-institutional clinical trial for assay validation in the context of use (COU) for FDA approval.

- 360 patient multi-institutional validation clinical trial.
- Blood drawn prior to standard of care radiation therapy for prostate cancer.
- Analyze plasma using the PC-Rad Test in a CLIA approved laboratory.

2. Critical Success Factors include:

- Test safety, tolerability and predictive value.
- Test production/manufacturing facility.
- Analysis and interpretation of test to referring physicians.
- Acceptance of cost and reimbursement in the US.
- PMA (Premarket Approval) by the FDA.
- Timely review and acceptance by medical organizations and physicians.

Intellectual Property Portfolio for Diagnostics

- **Diagnostic predictive biomarker patent application includes Georgetown University faculty and Shuttle Pharma scientists as co-inventors and has been filed by Georgetown University. Shuttle Pharma has obtained an exclusive license for development and commercialization of the PC-Rad Test.**
  - **Title: “Predictive Biomarkers for Adverse Effects of Radiation Therapy” ((Georgetown Reference) 2018-012)**
  - **U.S. Application No. 17/476,148 filed on September 15, 2021**
  - **PCT Application No. PCT/US2018/064924 filed on December 11, 2018**
  - **U.S. Provisional Application No. 62/597,172 filed on December 11, 2017**

Financials & Management

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Financial Overview

Shuttle Pharmaceuticals Cap Table as of September 30, 2023	
Common Stock	15,999,125
Fully Vested Restricted Stock Units (RSUs)	90,549
RSUs Outstanding	168,050
Warrants Outstanding	1,446,155
Total Shares on a Fully Diluted Basis	18,715,125

Capital Market Profile	
Exchange/Ticker	NASDAQ: SHPH
Closing Stock Price*	$0.35
52 Wk High/Low*	$0.35 - $2.75
Market Cap*	$5.6M
Cash Balance (9/30/23) [1]	$6.8M

[1] Including marketable securities

* As of 2/22/2024

Shuttle's Experienced Leadership Team

Anatoly Dritschilo, MD
CEO & Chairman

- Founder & CEO of Shuttle Pharma since 2012; Chairman, Board of Directors 2017
- Member, Board of Directors, Neopharm Inc. 1990
- Academic career: Georgetown University School of Medicine, Chairman, Department of Radiation Medicine, Medical Director Georgetown University Hospital, interim Director, Lombardi Cancer Center
- HDAC inhibitor patents

Peter Dritschilo, MBA
President & COO

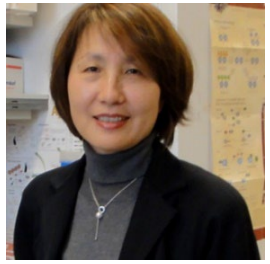
- Served as President & COO of Shuttle Pharma since 2012
- MBA George Washington University
- Radiation oncology administrator Rad America, Inova Health

Michael Vander Hoek , MHSA
CFO and VP Regulatory

- Served as CFO of Shuttle Pharma since 2019
- MHSA George Washington University
- Administrative Director, Lombardi Cancer Center

Tyvin Rich, MD
Medical Director

- Served as Medical Director of Shuttle Pharma since 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

- Served as Scientific Director of Shuttle Pharma since 2012
- Molecular Biology, University of Kansas; Radiation Biology, Georgetown University
- Professor of Radiation Medicine Georgetown University
- HDAC inhibitor patents and publications

Scott Grindrod, PhD
Principal Scientist
Laboratory Director

- Served as Principal Scientist and Laboratory Director of Shuttle Pharma since 2013
- Chemistry, University of Virginia and Medicinal Chemistry, Georgetown University
- HDAC inhibitor and Ropidoxuridine patents and publications

THANK YOU

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