Shuttle Pharmaceuticals Holdings, Inc.

Nasdaq: SHPH

Investor Presentation
August 2024

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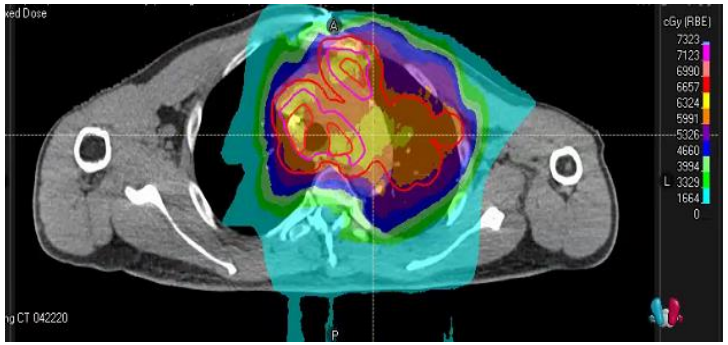
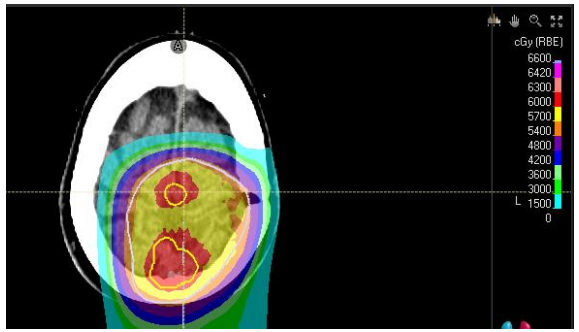
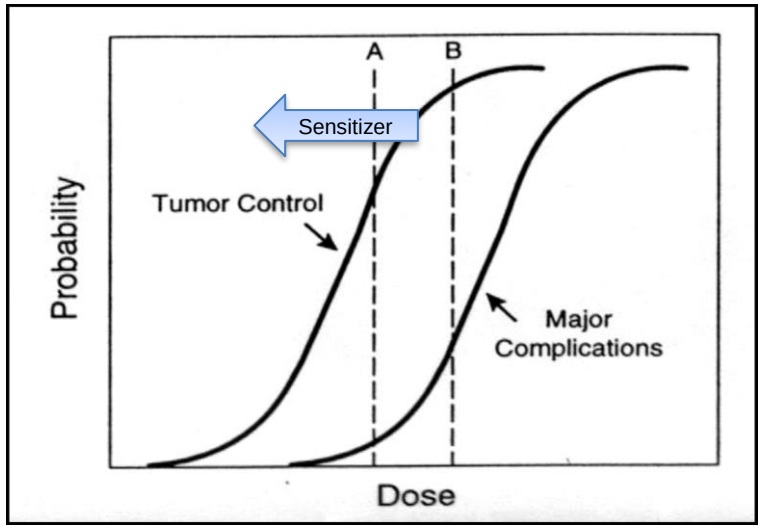
The Fundamental Problem of Radiation Therapy:

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







Sensitization of cancer cells to radiation therapy

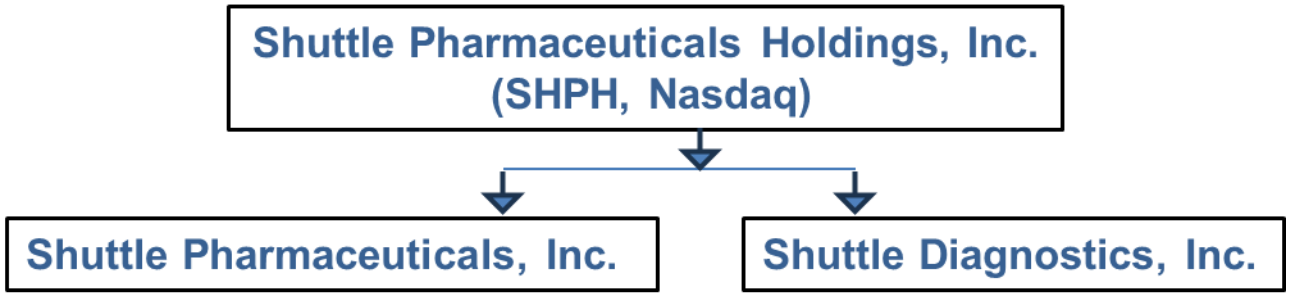
- The radiation dose determines cancer curability
- Adjacent normal tissues are dose-limiting
- Radiation sensitizers shift the dose-response to improve cancer control
- Currently available sensitizer drugs are mostly used “off-label”

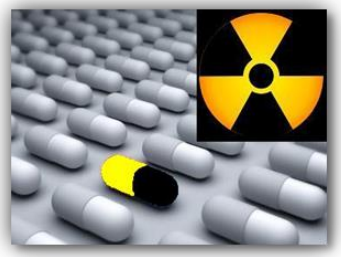
Activation of the immune response augments post-RT tumor responses

- Radiation of cancers induces antigens and activates cellular immunity
- Immune therapies using Pembrolizumab and Durvalumab have been shown to improve 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.

Radiation Sensitization

Cancer resistance to cure by radiation therapy, due to limitations presented by adjacent radiation sensitive normal tissues, can be overcome by Ropidoxuridine + RT

Radiation Sensitization and Immune Modulation

Selective HDAC6 inhibitors stimulate the innate immune system targeting radiation damaged cancer cells

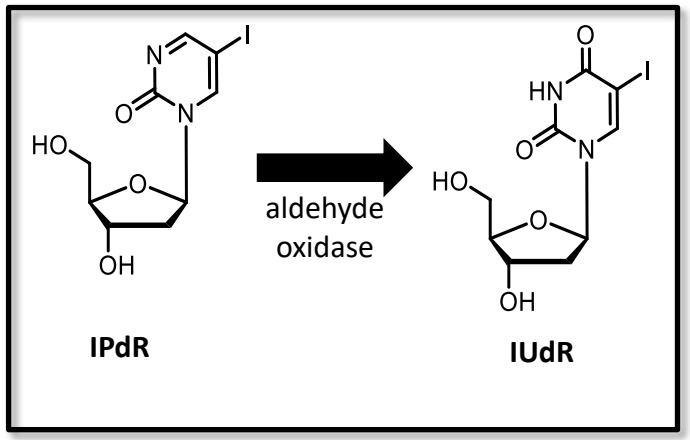
Diagnostics and Theranostics

- The PC-RAD blood test for use as a prostate cancer predictive biomarker
- The PSMA-B ligand for metastatic prostate cancer diagnosis and treatment

Ropidoxuridine (IPdR) – How does it work?

Ropidoxuridine (IPdR) is the prodrug of IUdR

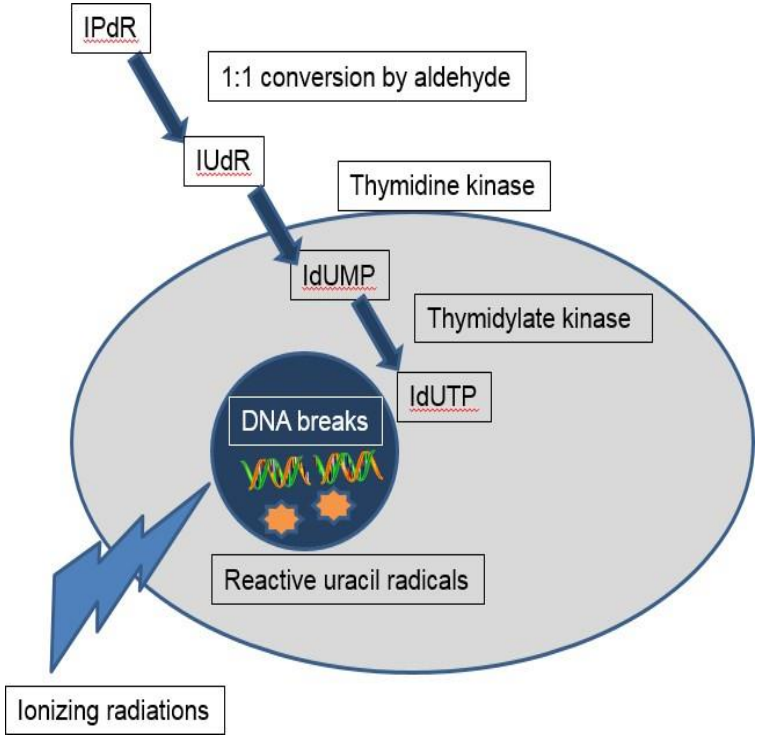
- IUdR is a powerful radiation sensitizer showing Phase II efficacy in NIH sponsored clinical trials in glioblastoma, anaplastic astrocytoma and sarcoma patients



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

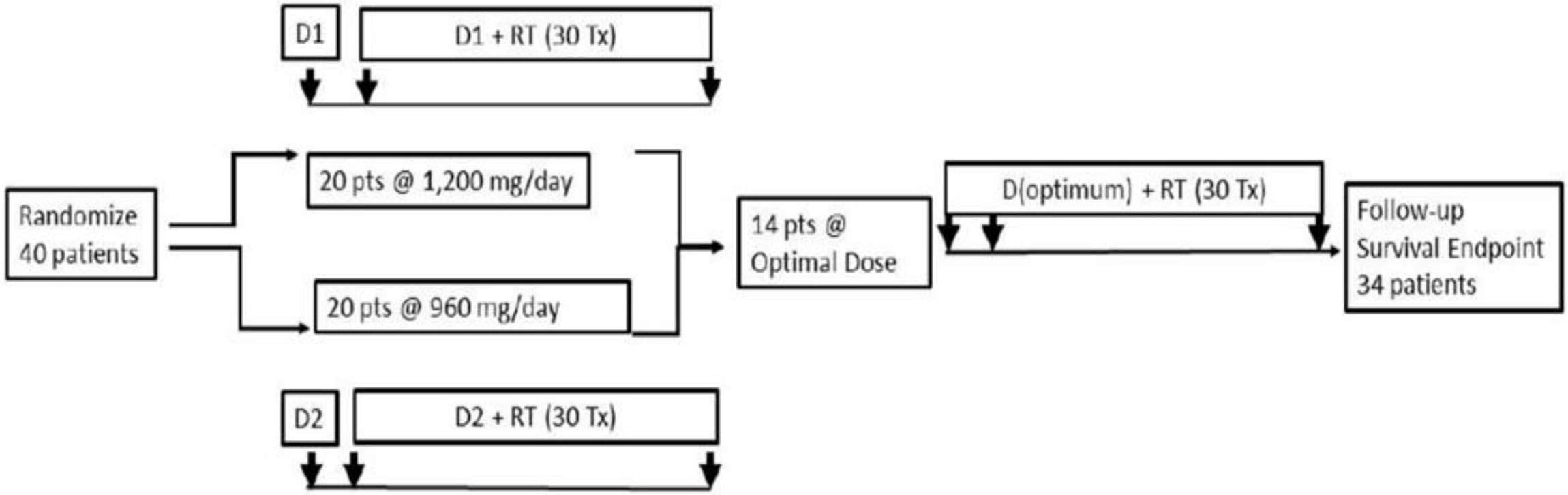
- IUdR requires intra-venous, constant infusion delivery, subject to adverse events
- IPdR is a prodrug, administered orally, and converted to IUdR for sensitizer effect
- NIH SBIR contract funding was awarded to Shuttle Pharma with a subcontract to Brown University/Rhode Island Hospital to perform the Phase I clinical trial.

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



Ropidoxuridine (IPdR) – Clinical Asset Development

- **Phase I and pharmacology study of Ropidoxuridine (IPdR) and RT (Clin Cancer Res, 2019).**
  - **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**
- **Phase II study of Ropidoxuridine + RT in IDH wild-type, methylation negative glioblastoma patients - IND has been approved and the FDA issued a safe to proceed letter.**



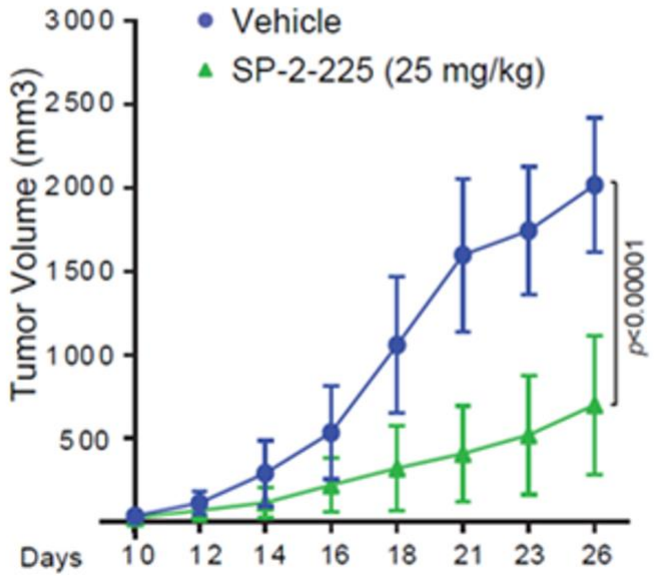
Ropidoxuridine (IPdR) – Phase II Update

Phase II study of Ropidoxuridine + RT . "Ropidoxuridine as a Radiosensitizer in Newly Diagnosed IDH-Wildtype Glioblastoma With Unmethylated MGMT Promoter" - ClinicalTrials.gov ID NCT06359379

- **Drug product (API) has been manufactured by TCG GreenChem and formulated into capsules by the University of Iowa Pharmaceuticals.**
- **Theradex Oncology, a U.S. based CRO has been engaged to monitor the al Phase II clinical trial.**
- **The IND has been approved and a safe to proceed letter has been issued by the FDA.**
- **Drug product (Ropidoxuridine capsules) are stored at Theradex for distribution to enrollment sites.**
- **Six academic cancer centers have been engaged for patient enrollment.**
- **Master and local IRB approvals have been obtained.**
- **Contract negotiations have been completed with 2 of the 6 planned enrollment sites - the University of Virginia and the University of Miami.**
- **Negotiations with the 4 remaining centers are expected to complete in September 2024.**
- **Enrollment is anticipated to require 12 to 18 months.**
- **Early results readout is anticipated in ~ 24 months.**

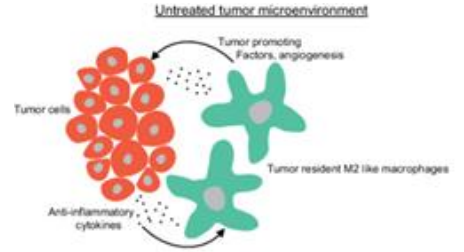
Pre-clinical Asset Development: Selective HDAC6 Inhibitor SP-2-225

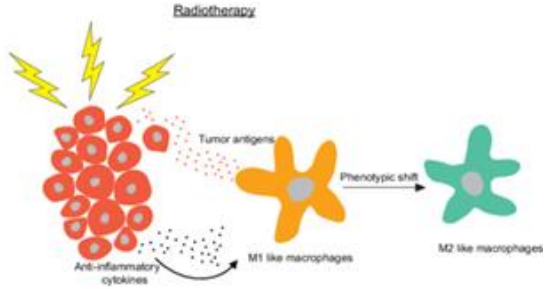
How does it work?

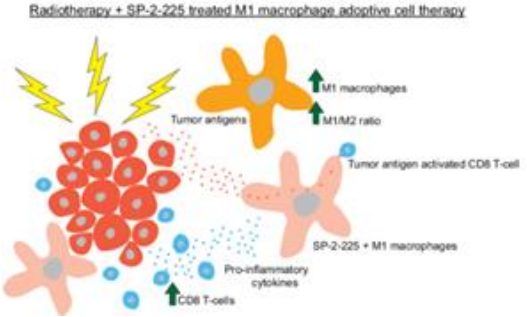


SP-2-225 inhibits HDAC6, prolongs macrophage polarization in M-1 state, resulting in an enhanced inflammatory response to immunogenic cancers and Irradiated tumors.

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.

Intellectual Property

Ropidoxuridine (radiation sensitizers)

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

Selective HDAC inhibitors (radiation sensitizers/immune modulators)

- **> 20 composition of matter HDAC inhibitor patents in the U.S., Canada and Europe.**
- **HDAC6 selective SP-2-225, Class I HDAC selective inhibitor SP-1-303.**
- **Patents wer invented by Shuttle Pharma's scientists and are Company property with no milestones or royalty requirements..**

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 - Priorities

THERAPEUTICS

- **Therapy Priority #1: 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**
- **Therapy Priority #2: 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**

DIAGNOSTICS

- **Diagnostic Priority #1: 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.**
- **Diagnostic Priority #2: Evaluate PSMA-B ligand 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.**
  - **Exploratory studies to synthesize and screen PSMA-B ligand-drug conjugates.**

Financial Overview

Shuttle Pharmaceuticals Cap Table as of March 31, 2024	
Common Stock	16,819,893
Fully Vested Restricted Stock Units (RSUs)	125,000
RSUs Outstanding	272,855
Warrants Outstanding	1,446,155
Total Shares on a Fully Diluted Basis	19,146,245

Capital Market Profile	
Exchange/Ticker	NASDAQ: SHPH
Closing Stock Price*	$0.42
52 Wk High/Low*	$0.35 - $2.75
Market Cap*	$7.0M
Cash Balance (3/31/23) [1]	$4.2M

[1] Including marketable securities

* As of 5/22/2024

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

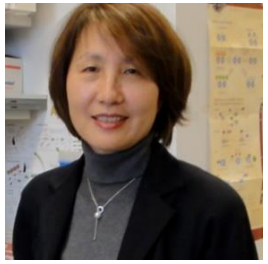
- President & COO of Shuttle Pharma 2012
- CFO Shuttle Pharma 2012-2019
- Co-Founder Shuttle Pharma 2012
- Radiation oncology administrator:
- Rad America, Inova Health
- MBA George Washington University

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 yrears 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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