Shuttle Pharmaceuticals Holdings, Inc.
Nasdaq: SHPH

2024 ANNUAL REPORT

Pursuing a Cure for Cancer

We are developing novel therapies designed to increase cancer cure rates, prolong patient survival, and improve quality of life.

DEAR SHAREHOLDERS

It is with great excitement that I write to review the key milestones that have been reached over the past year and those that remain in focus to advance Shuttle Pharma's mission to improve outcomes for cancer patients receiving radiation therapy (RT).

LEAD PROGRAM LAUNCHED WITH ENROLLMENT MEETING ALL EXPECTATIONS

The biggest milestone achieved this past year was the successful launch of our Phase 2 trial of Ropidoxuridine and RT for treatment of patients with glioblastoma. We officially reached that milestone in November 2024 when the first patients had been enrolled and treated at three of the six cancer center affiliates: UVA Cancer Center, Miami Cancer Institute, part of Baptist Health South Florida, and the John Theurer Cancer Center at Hackensack University Medical Center.

Since the first patients were dosed, **enrollment into the clinical trial has been robust and has met all expectations.** As of writing this letter, we have achieved 43% enrollment in the initial randomized phase of the clinical trial with a total enrollment of 17 of the initial 40 patients. Further, 11 of the 40 patients have completed all seven cycles. Our objective is to finalize enrollment later this year with follow up and data read out in 2026.

Leading up to trial commencement, we **successfully onboarded all six nationally recognized, East Coast cancer centers.** The six centers were chosen for their recognized state-of-the art cancer care and the availability of patients presenting with the most aggressive form of brain tumors– IDH wild-type, methylation negative glioblastoma, the target of the clinical trial.

As a reminder, the Phase 2 clinical trial design initially randomizes 40 patients into two different dose levels of drug, with 20 patients receiving 1,200 mg/day and 20 patients receiving 960 mg/day, to determine an optimal dose for use in glioblastoma patients in combination with RT. After the optimal dose is identified, 14 additional patients will be enrolled at the optimal dose to reach statistical significance with the end-point demonstrating increased survival as compared to historical controls.

This clinical trial is critical to the broader radiation therapy industry as we look to leverage radiation sensitizers to increase cancer cure rates, prolong patient survival and improve quality of life for patients suffering from glioblastoma. I look forward to continued trial execution as we aim to improve the lives of millions of patients impacted by cancer and to bring hope to patients and families around the world.

ADVANCEMENT OF A ROBUST DEVELOPMENT PORTFOLIO

Our primary focus is on our lead therapeutic Ropidoxuridine program. However, it remains important to understand the depth of development stage assets across both cancer **Therapeutics** and **Diagnostics**.

THERAPEUTICS

Within Therapeutics, after Ropidoxuridine, the second priority has been focused on our HDAC6 selective inhibitor SP-2-225. During the past year, we have contracted with Dr. Alejandro Villagra's laboratory at Georgetown University to perform in vivo studies of HDAC6 inhibition in 4T1 syngeneic mouse breast cancers. **Tumor growth delay** has been observed, and **validation experiments** have been completed. SP- 2-225 is ready for IND-enabling studies followed by Phase I clinical testing.

Development of other preclinical assets, including our next generation radiation sensitizer formulation of Ropidoxuridine / Tipiracil and our Class I selective HDAC inhibitor for **ER+ breast cancer**, will be prioritized as funds become available. In addition, we plan to submit applications for NIH funding and seek collaborations or joint ventures to support further development of selected preclinical assets.

DIAGNOSTICS

Our Shuttle Diagnostics subsidiary **aims to develop pretreatment diagnostic blood tests and imaging agents for prostate cancer patients**. The PC-Rad test was developed for predicting outcomes following radiation therapy for localized prostate cancer and the PSMA-B ligand is a theranostic molecules offering diagnosis and therapeutics capability for metastatic prostate cancer.

The intellectual property underlying the **PC-Rad Test predictive biomarker** technology was developed by a collaboration of Shuttle Pharma and Georgetown University scientists through analytical validation and is ready for clinical validation to seek FDA approval as a medical device. Current plans focus on initiation of the clinical trial for clinical validation of the PC-Rad Test by an investigator-initiated clinical trial, working with colleagues at MedStar-Georgetown University Hospital, and expanding to a multi-institutional clinical trial as resources become available.

For our **PSMA-B development program**, we have entered into a sponsored research agreement with the University of California, San Francisco (UCSF) to advance pre-clinical development as a potential diagnostic and therapeutic, or theranostic, molecule. In a discovery project to develop a novel, boron-containing PSMA ligand to enhance proton radiation therapy of prostate cancer, we observed that the PSMA-Ba molecule containing boron and demonstrating nanomolar binding activity to PSMA also offered the potential for imaging metastatic prostate cancer. **Preclinical evaluations have been initiated** to explore the PSMA-B ligand as a potential prostate cancer sensitizer in combination with proton therapy, as well as a PET diagnostic reagent and as a targeted prostate cancer therapeutic. The agreement with UCSF will support further preclinical testing in a mouse model of prostate cancer for its potential to bind to prostate cancer deposits in mice.

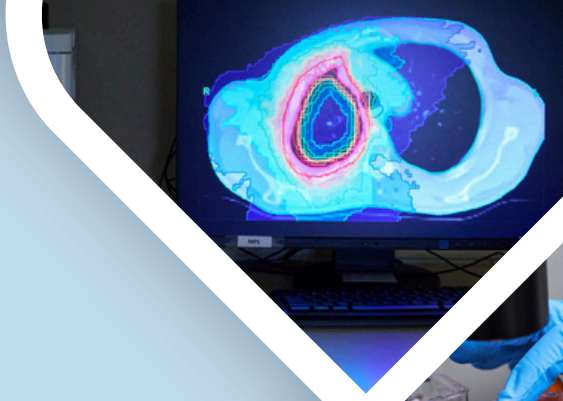
Our intellectual property within both diagnostic programs (PC-Rad and PSMA-B ligand) offers an opportunity for further development through a potential Shuttle Diagnostics spin-out.

ENHANCED BUSINESS FOCUS

With scientific and clinical trial activities accelerating, Christopher Cooper has been appointed as interim Chief Executive Officer, focused on enhancing capital markets and business capabilities. Christopher brings a wealth of business experience which, when balanced with the inherent scientific expertise of the Shuttle Pharma team, should allow for a more effective executive structure to inspire confidence going forward.

We have also appointed three new members to our board of directors (George Scorsis, Oleh Nabyt and Joseph Tung), offering **business and legal backgrounds to help guide the Company going forward.** In connection with appointments of new members, Dr. Milton Brown, Dr. Chris Senanayake, Dr. Bette Jacobs and Mr. Joshua Schafer resigned from their positions. I personally thank Drs. Brown, Senanayake, Jacobs and Mr. Schafer for their contributions to the company.

As a pre-revenue discovery and developmental company, we are dependent on expanding our access to the capital markets, and most recently, we completed a $5.75 million straight common stock offering in March 2025 to support the Phase 2 clinical trial for Ropidoxuridine and RT, for marketing and advertising services, and for working capital and general corporate purposes.



OUR WORK. OUR PURPOSE.

At Shuttle Pharma, **our mission is to launch the next generation of drugs to improve outcomes and achieve more cures for cancer patients** undergoing radiation treatments. We acknowledge that this will not be an easy task and will require **dedication, extreme effort, and expertise**.

Through teamwork and strategic collaboration, **we believe in our ability to make a meaningful difference** in the lives of cancer patients. By pushing scientific boundaries and working together, we aim to improve the lives of millions impacted by cancer and bring hope to patients and families around the world.

I thank our team and investors for continued support as Shuttle Pharma's drugs achieve scientific milestones on a path to commercialization and clinical application.

Sincerely yours,

Anatoly Dritschilo

Anatoly Dritschilo, MD
Chairman of the Board of Directors, Shuttle Pharmaceuticals Holdings, Inc.

SHUTTLE
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Nasdaq: SHPH

Shuttle Pharmaceuticals Holdings, Inc.
401 Professional Drive
Suite 260
Gaithersburg, MD 20879

240-403-4212
info@shuttlepharma.com