Shuttle Pharmaceuticals Provides Fiscal Year 2022 Corporate Update

ROCKVILLE, Md., March 15, 2023 — Shuttle Pharmaceuticals Holdings, Inc. (Nasdaq: SHPH), a discovery and development stage specialty pharmaceutical company focused on improving outcomes for cancer patients treated with radiation therapy (RT), today provided a corporate update in connection with the filing of its Annual Report on Form 10-K for the year ended December 31, 2022.

Recent Highlights

- Completed an initial public offering ("IPO") raising gross proceeds of $11.5 million, inclusive of the overallotment option, listing its common stock on the Nasdaq Capital Market.
- Closed on private placement of $4.3 Million of Senior Secured Convertible Note and Warrants to purchase 1.018 million shares of common stock in exchange for $4.0 million investment.
- Entered into agreements with TCG GreenChem, Inc. and UI Pharmaceuticals for drug manufacture and formulation development of Ropidoxuridine, the Company's lead clinical sensitizer drug candidate, for use in the Company's upcoming Phase II clinical trial evaluating Ropidoxuridine in combination with radiation therapy for the treatment of glioblastoma.
- Engaged Theradex Oncology, a leading clinical research organization, to help prepare for its upcoming clinical study of Ropidoxuridine.
- Entered into an agreement to lease new laboratory and office space, commencing in June 2023, to assist in furthering the development of the Company's lead drug candidates and accelerate broader diagnostic capabilities on predictive biomarkers.
- Published manuscripts discussing prostate cancer cell lines derived from African

American men for precision medicine and immune responses taking place in patients after radiation therapy for cancer.
- Awarded patents in the U.S. and Hong Kong for its radiation sensitizing HDAC inhibitor technology platform.
- Appointed Dr. Bette Jacobs to its Board of Directors as an independent director.
- Rang the Nasdaq opening bell in January 2023.
- At December 31, 2022, the Company's Cash balance was $8.4 million. Subsequently, on January 11, 2023, the Company closed on the $4.0 million private placement.

"We continue to execute on the necessary steps to advance Ropidoxuridine, our lead clinical sensitizer drug candidate, towards the commencement of our upcoming Phase II clinical trial in brain cancer patients undergoing radiation therapy with an expectation of final submission to the FDA at the end of the second quarter of 2023," commented Shuttle Pharma's Chairman and CEO, Anatoly Dritschilo, M.D. "Since our August 2022 IPO, we have moved swiftly to advance drug manufacturing agreements, prepare our IND application for the planned Phase II clinical study of Ropidoxuridine and radiation therapy, and lease new laboratory space to complement the development of the Company's lead drug candidates and accelerate broader diagnostic capabilities on predictive biomarkers. Importantly, we anticipate that our improved balance sheet will provide us with sufficient capital to fund operations into the 4th quarter of 2025, which will allow for the advancement of Ropidoxuridine and our HDAC inhibitors to reach additional important milestones. I look forward to 2023 with enthusiasm as we work to complete a number of key upcoming milestones on the horizon."

Radiation Therapy Sensitizer Platform

Radiation therapy is a proven modality for cancer treatment. By developing radiation sensitizers, Shuttle Pharma aims to increase cancer cure rates, prolong patient survival and improve quality of life when radiation is used as a primary treatment, or in combination with, surgery, chemotherapy and immunotherapy.

Modern oncology incorporates multi-modality strategies that use combinations of surgery, chemo or immunotherapy, and radiation to treat cancers. Radiation therapy requires delivery and shaping of high doses of radiation energy to tumors to kill or slow the growth of cancer cells by damaging their cellular DNA. State-of-the-art technologies to deliver the radiation doses include image guided treatments with linear accelerators and particle radiation with protons. However, radiation therapy of adjacent healthy tissues can lead to injuries of normal organs. The addition of radiation sensitizers allows preferential increased killing of cancer cells.

Currently, there is only one drug on the market approved by the FDA as a radiation sensitizer. However, that drug has a host of side effects that limit its utility. Other drugs are used "off

label” by radiation oncologists, but these often have additional side effects. There is an urgent need for an effective radiation sensitizer with low toxicity for use in combination with radiation therapy.

The Company’s lead candidate, Ropidoxuridine, is an orally available prodrug, that once ingested, metabolizes into iododeoxyuridine, a pyrimidine analog, that has been recognized as a radio sensitizing agent since the 1960s. The Company is advancing its planned Phase II clinical trial of Ropidoxuridine in brain cancer patients undergoing radiation therapy for glioblastoma. Shuttle is currently preparing the Investigational New Drug application for the study with an expectation of final submission to the FDA at the end of the second quarter of 2023.

Beyond Ropidoxuridine, Shuttle is also developing a platform of HDAC inhibitors (SP-1-161, SP-2-225 and SP-1-303), with SP-2-225 being Shuttle’s lead HDAC inhibitor for preclinical development. SP-2-225 has effects on the regulation of the immune system. The interactions of RT with the immune response to cancers are of great current interest, offering insight into potential mechanisms for primary site and metastatic cancer treatment. The Company is currently advancing drug manufacture and IND-enabling studies to enable a Phase I clinical trial in 2024.

Various sources have estimated that more than 800,000 patients are treated annually in the U.S. with radiation therapy for their cancers. About 50% are treated for curative purposes and the balance for palliative care. The market opportunity for radiation sensitizers lies with the 400,000 patients treated with curative intent. Based on a rough estimate of a course of radiation sensitizing brand drug therapy, which are used off label at this time, the potential market size is estimated to be in excess of $4.0 billion annually.

Manufacturing Agreements

In September 2022, the Company announced it entered into an agreement with TCG GreenChem, Inc. to manufacture Ropidoxuridine, the Company’s lead clinical sensitizer drug candidate, for use in formulating the drug product for testing in clinical trials of Ropidoxuridine and RT of cancers. The agreement with TCG GreenChem allows the Company to advance its clinical research, including its proposed Phase II clinical trials, to establish the data necessary for the FDA to determine efficacy in treating brain tumors, sarcomas and pancreatic cancers, diseases that offer potential for orphan designations. In conjunction with manufacturing Ropidoxuridine, TCG GreenChem will perform process research, development and optimization work for Shuttle Pharma related to Ropidoxuridine and create working standards of starting materials and intermediates to support the qualitative/quantitative analysis of the drug reaction progress, determination of impurities, total mass balance and assay yields of the reactions. Shuttle Pharma will own all intellectual property and improvements developed through the Manufacturing Agreement.

In March 2023, Shuttle signed an agreement with the University of Iowa (UI) Pharmaceuticals for formulation development and clinical batch manufacture of drug capsules of Ropidoxuridine. This is expected to be the final step required in the drug manufacturing process for use in the Company's upcoming Phase II clinical trial evaluating Ropidoxuridine in combination with radiation therapy for the treatment of glioblastoma. UI Pharmaceuticals offers pharmaceutical product development, manufacturing, and testing services for tablets, capsules, and non-sterile powder, semisolid, and liquid products. Because UI Pharmaceuticals is registered with the FDA as a Drug Product Manufacturing and Testing Facility, they have the capability to produce and test products intended for both clinical studies and commercial sales.

Engagement of Theradex Oncology

In November 2022, Shuttle announced it had engaged Theradex Oncology, a leading clinical research organization ("CRO"), to help prepare for its upcoming clinical study of Ropidoxuridine. Specifically, Theradex Oncology will assist the Company in meetings with the FDA and preparation of the IND (Investigational New Drug) application for the planned Phase II clinical study of Ropidoxuridine and radiation therapy. Theradex's expertise in regulatory and statistical design is particularly helpful in meeting FDA requirements and providing guidance in study design and statistical support for the clinical trial.

Theradex Oncology has provided full oncology clinical trial services in the U.S. and Europe for over three decades. Meg Valnoski, president of Theradex, will be directly involved in the regulatory support provided to Shuttle Pharmaceuticals, working closely with a diverse team of experts to ensure the successful execution of clinical trials.

Laboratory Space Expansion

The Company entered an agreement to lease new laboratory and office space, commencing in June 2023, to complement the development of the Company's lead drug candidates and accelerate broader diagnostic capabilities on predictive biomarkers. The new laboratory space, located in Gaithersburg, Maryland, is located within the Maryland Biotech Corridor.

Publications

In December 2022, Shuttle Pharma announced the publication of a manuscript discussing prostate cancer cell lines derived from African American men for precision medicine. The manuscript, titled "Novel paired normal prostate and prostate cancer model cell systems derived from African American patients," by Dr. Mira Jung, was published in Cancer Research Communications, a journal affiliated with the American Association for Cancer Research (AACR), the premier international cancer research society. Unique cell cultures were developed by a collaborative effort of Shuttle Pharma and Georgetown University scientists and clinicians in a "Moonshot" project funded by the NIH SBIR program to address prostate

cancer health disparities in African American men. Prostate cancer is the most frequently diagnosed solid malignancy in men. African American (AA) men are at greater risk for developing prostate cancer, and experience higher mortality rates, as compared to Caucasian American (CA) men. However, mechanistic studies to understand this health disparity have been limited by the lack of relevant in vitro and in vivo models. There is an urgent need for preclinical cellular models to investigate molecular mechanisms underlying prostate cancer in AA men. By collecting clinical specimens from radical prostatectomies of AA patients, ten paired tumor-derived and normal epithelial cell cultures were established from the same donors and cultivated to extend the growth under "conditional reprogramming (CR)."

In January 2023, Shuttle Pharma announced the publication of a manuscript discussing immune responses taking place in patients after radiation therapy for cancer. The manuscript, titled, "Radiation therapy induces innate immune responses in patients treated for prostate cancers," by Dr. Amrita K Cheema, was published in Clinical Cancer Research, a journal affiliated with the American Association for Cancer Research (AACR), the premier international cancer research society. The report provided insight into the immune response taking place in patients after radiation therapy for cancer. These data inform potential development of biomarkers of radiation response and therapeutic strategies for sequencing radiation and immune therapy modalities for cancer treatment.

Patent Awards

In September 2022, Shuttle Pharma announced it had been awarded patents in the U.S. and Hong Kong for its radiation sensitizing HDAC inhibitor technology platform, which is focused on reducing side effects and improving outcomes for cancer patients treated with radiation therapy (RT). Histone deacetylase (HDAC) inhibitors have been described as "a novel class of drugs that target enzymes involved in regulation of critical cellular functions that can inhibit cancer growth and activate cellular immunity," according to Scott Grindrod, PhD, lead inventor and Laboratory Director at Shuttle Pharma.

Treatment with HDAC inhibitors allows regulation of gene expression by blocking HDAC enzyme activity and allowing genes to be "turned on" to express proteins involved in regulation of the cell cycle, DNA damage response and immune activation. Inhibiting HDAC enzymes can turn on tumor suppressor genes to help control cell division and slow down cancer progression. Non-cytotoxic, highly selective inhibitors target the histone deacetylase 6 (HDAC6) enzyme to stimulate the immune system for applications in the treatment of cancers, neurological diseases and immunological disorders.

About Shuttle Pharmaceuticals

Founded in 2012 by faculty members of the Georgetown University Medical Center, Shuttle Pharma is a discovery and development stage specialty pharmaceutical company focused on

improving the outcomes for cancer patients treated with radiation therapy (RT). Our mission is to improve the lives of cancer patients by developing therapies that are designed to maximize the effectiveness of RT while limiting the side effects of radiation in cancer treatment. Although RT is a proven modality for treating cancers, by developing radiation sensitizers, we aim to increase cancer cure rates, prolong patient survival and improve quality of life when used as a primary treatment or in combination with surgery, chemotherapy and immunotherapy. For more information, please visit our website at www.shuttlepharma.com.

Safe Harbor Statement

Statements in this press release about future expectations, plans and prospects, as well as any other statements regarding matters that are not historical facts, may constitute “forward-looking statements.” These statements include, but are not limited to, statements concerning the development of our company. The words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “will,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including factors discussed in the “Risk Factors” section of Shuttle Pharma’s Annual Report on Form 10-K for the year ended December 31, 2022, filed with the SEC on March 15, 2023. Any forward-looking statements contained in this press release speak only as of the date hereof and, except as required by federal securities laws, Shuttle Pharmaceuticals specifically disclaims any obligation to update any forward-looking statement, whether as a result of new information, future events or otherwise.

Shuttle Pharmaceuticals
Anatoly Dritschilo, M.D., CEO
240-403-4212
info@shuttlepharma.com

Investor Contacts
Lytham Partners, LLC
Robert Blum
602-889-9700
shph@lythampartners.com

View original content to download multimedia:https://www.prnewswire.com/news-releases/shuttle-pharmaceuticals-provides-fiscal-year-2022-corporate-update-301772572.html

SOURCE Shuttle Pharmaceuticals Holdings, Inc.