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Processa Pharmaceuticals

Processa Successfully Identifies Next Generation Capecitabine Dosage Regimens for Phase 2B Trial

Next Generation Capecitabine (NGC) Dosage Regimens Have Been Identified In The Ongoing Phase 1B Trial With Potentially Better Safety And Efficacy Profiles Than Existing Chemotherapy

- These NGC dosage regimens are significantly more potent than existing FDA-approved capecitabine therapy based on a greater systemic and tumor exposure to 5-Fluorouracil (5-FU), the major metabolite of capecitabine.
- These NGC dosage regimens form less of the metabolites that only cause dose-limiting side effects with no tumor-killing properties.
- Processa will meet with FDA in 2023 to confirm that the design of the Phase 2B trial conforms with the FDA's Project Optimus Oncology initiative to identify optimal dosing regimens while moving away from the maximum tolerated dosing approach of the past.
- In 2023 Processa plans to begin enrolling patients into the Phase 2B trial to identify the regimens that improve the efficacy-safety profile over present therapy.

HANOVER, MD, Nov. 01, 2022 (GLOBE NEWSWIRE) -- Processa Pharmaceuticals, Inc. (Nasdaq: PCSA), a diversified clinical-stage company developing products to improve survival and/or the quality of life for patients who have an unmet medical need condition, announces positive results from its ongoing Next Generation Capecitabine (NGC) Phase 1B trial. The data collected has allowed Processa to estimate the timeline of dihydropyrimidine dehydrogenase (DPD) irreversible inhibition and the formation of new DPD after PCS6422 administration. NGC regimens (i.e., a variety of PCS6422 regimens combined with a variety of capecitabine regimens) were also identified that are safe with different systemic and tumor exposure profiles to 5-FU. These findings will allow Processa to evaluate multiple regimens with varying 5-FU tumor exposures in the Phase 2B trial for the purpose of identifying the NGC regimens that provide an improved efficacy-safety profile over present therapy.

During the first 24 to 72 hours after administration of PCS6422 in the Phase 1B trial, less than 10% of the 5-FU was converted into the metabolites that only cause side effects (i.e., catabolites), significantly less than the 80% reported for FDA-approved capecitabine. The potency of NGC (estimated from 5-FU systemic exposure) was approximately 50-times greater than the potency of FDA-approved capecitabine. In addition, the half-life of 5-FU after the initial administration of PCS6422 and capecitabine was found to be significantly greater at 2 to 6 hours versus the typical 5-FU half-life of approximately 45 minutes after capecitabine administration.

Since 5-FU exposure is dependent on both the PCS6422 regimen and the capecitabine regimen, Processa has identified both NGC regimens that are safe as well as regimens that cause dose-limiting toxicities as was seen with one patient in the Phase 1B trial who had progressive stage 4 cancer. This patient had Grade 4 neutropenia, was admitted to the

hospital, and subsequently died.

Dr. David Young, President and CEO of Processa, stated, “We have identified NGC regimens that have potency significantly greater than existing therapy and no dose-limiting side effects, unlike existing capecitabine therapy where approximately 25- 60% of the patients require dose modifications or discontinuation. In addition, we understand the effect of different NGC regimens on the timeline of DPD irreversible inhibition and a patient’s production of new DPD, allowing us to better define the relationship between various NGC dosage regimens, 5-FU exposure, and the safety of NGC.”

Dr. Young added, “The next step will be to demonstrate in a Phase 2B trial that these NGC regimens also have better efficacy than existing therapy and, therefore, provide a significant improvement in the benefit-risk profile over existing therapy. We plan to use a Phase 2B trial to determine which regimens provide this improved efficacy-safety profile over present therapy using the principles of the FDA’s Oncology Project Optimus initiative to help guide us in the design of the trial. In 2023 Processa plans to meet with FDA to discuss the design of our Phase 2B trial and initiate the trial.”

Next Generation Capecitabine

Next Generation Capecitabine (NGC) is a combination of a PCS6422 regimen and a separate capecitabine regimen. Capecitabine is a fluoropyrimidine, like 5-Fluorouracil (5-FU) the major metabolite of capecitabine, that remains the cornerstone of treatment for many types of cancers in an estimated two million patients annually. Capecitabine is an oral pro-drug of 5-FU and approved as first-line therapy for metastatic colorectal and breast cancer. The adverse effects of capecitabine such as the development of Hand-Foot Syndrome from 5-FU catabolites (e.g., α-fluoro-β-alanine (F-Bal)) and neutropenia from 5-FU anabolites (e.g., phosphate metabolites) can have severe adverse effects on a patient’s daily activities, quality of life, and potentially requiring dose interruptions-adjustments or therapy discontinuation, all resulting in suboptimal tumor therapy.

PCS6422 is an oral, potent, selective, and irreversible inhibitor of dihydropyrimidine dehydrogenase (DPD), the enzyme that rapidly metabolizes 5-FU into catabolites which can cause dose-limiting side effects. The formation of 5-FU anabolites in cancer cells and normal cells is not dependent on DPD.

By combining the regimens of PCS6422 and capecitabine, the change in 5-FU metabolism and, therefore, elimination results in an increase in the potency of capecitabine as determined by the systemic exposure of 5-FU per mg of capecitabine administered. This results in requiring less capecitabine to kill cancer cells and to treat each patient. To date, Processa has found that the irreversible inhibition of DPD by PCS6422 can alter the elimination of 5-FU making NGC significantly more potent (greater than 50-times more potent) and potentially leading to higher levels of the anabolites which can kill replicating cancer and normal cells causing dose limiting side effects such as neutropenia. By administering NGC to cancer patients, the balance between anabolites and catabolites changes depending on the dosage regimens of PCS6422 and capecitabine used, making the efficacy-safety profile of NGC different than that of FDA-approved capecitabine and requiring further evaluation of the PCS6422 and capecitabine regimens to determine the optimal Next Generation Capecitabine regimens for patients.

The projected market for NGC is $500 million to $1 billion in the U.S. for the treatment of colorectal cancer and over $1 billion within the U.S. for the treatment of the many cancers that capecitabine is used. The potential worldwide market for NGC for colorectal cancer exceeds $1 billion.

About Processa Pharmaceuticals, Inc.

The mission of Processa is to develop products with existing clinical evidence of efficacy for patients with unmet or underserved medical conditions who need treatment options that improve survival and/or quality of life. The Company uses its Regulatory Science Approach criteria when selecting drugs for development to achieve high-value milestones effectively and efficiently. Active clinical pipeline programs include: PCS6422 (metastatic colorectal cancer, breast cancer), PCS12852 (gastroparesis, functional constipation), and PCS499 (ulcerative necrobiosis lipoidica). Members of the Processa development team have been involved with more than 30 approvals for indications in almost every division of the FDA (including drug products targeted to orphan disease conditions) and more than 100 FDA meetings throughout their careers. For more information, visit our website at www.processapharma.com.

Forward-Looking Statements

This release contains forward-looking statements. The statements in this press release that are not purely historical are forward-looking statements that involve risks and uncertainties. Actual future performance outcomes and results may differ materially from those expressed in forward-looking statements. Please refer to the documents filed by Processa Pharmaceuticals with the SEC, specifically the most recent reports on Forms 10-K and 10-Q, which identify important risk factors which could cause actual results to differ from those contained in the forward-looking statements.

For More Information:
Michael Floyd
mfloyd@processapharma.com
(301) 651-4256

Patrick Lin
(925) 683-3218
plin@processapharma.com

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