Wellstat Announces FDA Approval of VISTOGARD® (Uridine Triacetate), the First Antidote to Treat Overdoses and Early-Onset Severe Toxicities Due to 5-Fluorouracil (5-FU) and Capecitabine Chemotherapies

Gaithersburg, MD - December 11, 2015 - Wellstat Therapeutics Corporation announced today that the US Food and Drug Administration (FDA) has approved VISTOGARD® (uridine triacetate) as the first and only antidote for emergency treatment of adult and pediatric patients following an overdose of the chemotherapy agents 5-Fluorouracil (5-FU) or capecitabine regardless of the presence of symptoms, or to treat patients who exhibit early-onset, severe or life-threatening toxicity affecting cardiac or central nervous system, and/or early-onset, unusually severe adverse reactions within 96 hours after the end of treatment with 5-FU or capecitabine.

VISTOGARD will be marketed, sold, and distributed in the US by Wellstat’s commercialization partner BTG plc.

“Wellstat has developed VISTOGARD to help patients treated with 5-FU or capecitabine who develop severe or life threatening toxicity or experience an overdose. It is the only treatment approved by the FDA for early onset severe toxicities or 5-FU overdose and now will be available to the thousands of patients impacted by this condition. This is Wellstat’s second FDA approval in 2015 which highlights the extraordinary work of our research and development teams,” said Samuel J. Wohlstadter, CEO of Wellstat Therapeutics.

The drugs 5-FU and capecitabine are essential components of combination anticancer regimens that include other chemotherapy agents or radiation to treat solid tumors including those of the colon, stomach, pancreas, breast, head and neck. Each year 250,000 to 300,000
patients in the U.S. receive multiple treatments with 5-FU, typically administered at or near what is considered the maximum tolerated dose. Life-threatening or even lethal 5-FU or capecitabine toxicities can occur when the drug is administered at a dose or rate greater than intended, or when a patient has unusual susceptibilities to the toxic effects of these drugs due to genetic mutations, impaired clearance or other factors. It is estimated that ten to twenty percent of patients treated with 5-FU or capecitabine develop severe or life-threatening toxicity or experience an overdose, and that approximately 0.5% of patients die from such toxicity.

In two open label clinical studies involving 135 patients, the survival rate for patients treated with VISTOGARD was 96 percent following an overdose of 5-FU or capecitabine and in patients who had developed early-onset severe toxicities, including cardio- and/or neuro-toxicity and/or gastrointestinal and hematologic toxicities following administration of these chemotherapy drugs at intended doses. In contrast, the survival rate was 16 percent in 25 historical case reports of patients overdosed with 5-FU. In addition, 33 percent of cancer patients treated with VISTOGARD resumed their chemotherapy in less than 30 days.

“VISTOGARD is the first and only antidote for 5-FU and capecitabine overdose and for early-onset, severe, life-threatening toxicities approved by the FDA for treatment of adults and children. It addresses an important unmet medical need and has an excellent safety profile. Timely treatment with VISTOGARD saves lives and helps patients continue fighting their cancer,” said Michael Bamat, PhD, Vice President of Research and Development at Wellstat Therapeutics.

**VISTOGARD Clinical Development Program**

The FDA approval of VISTOGARD is based on data from a development program in 135 patients designed to demonstrate the efficacy and safety of a single course of 10 grams given orally every six hours for a total of 20 doses (patients in the studies had either received an overdose of 5-FU or capecitabine, or presented with severe or life-threatening toxicities within 96 hours following the end of 5-FU or capecitabine administration). In clinical studies, overall survival of patients with 5-FU toxicity receiving VISTOGARD was 96 percent, compared with 16 percent in historical cases employing standard supportive care measures. VISTOGARD also helped patients resume chemotherapy sooner, with 33 percent resuming their cancer treatment within 30 days.

Adverse events that occurred in greater than 2 percent of patients were vomiting (10%), nausea (5%) and diarrhea (3%).

Following today’s approval, VISTOGARD will be made available to the US market as soon as possible. In the interim, physicians treating patients in need of VISTOGARD treatment are encouraged to follow the current emergency access protocol and contact Wellstat.

Wellstat Therapeutics
Selected Important Safety Information for VISTOGARD (Uridine Triacetate) oral granules

INDICATION
VISTOGARD is indicated for the emergency treatment of adult and pediatric patients:

- following a fluorouracil or capecitabine overdose regardless of the presence of symptoms, or
- who exhibit early-onset, severe or life-threatening toxicity affecting the cardiac or central nervous system, and/or early-onset, unusually severe adverse reactions (e.g., gastrointestinal toxicity and/or neutropenia) within 96 hours following the end of fluorouracil or capecitabine administration.

Limitations of use:

- VISTOGARD is not recommended for the non-emergent treatment of adverse reactions associated with fluorouracil or capecitabine because it may diminish the efficacy of these drugs.
- The safety and efficacy of VISTOGARD initiated more than 96 hours following the end of fluorouracil or capecitabine administration have not been established.

IMPORTANT SAFETY INFORMATION

- In clinical studies, adverse reactions occurring in > 2% patients receiving VISTOGARD were vomiting (10%), nausea (5%) and diarrhea (3%).
- One patient receiving uridine triacetate experienced grade 3 nausea and vomiting.

Please see full Prescribing Information.

About VISTOGARD (uridine triacetate) oral granules

VISTOGARD (uridine triacetate) is an orally administered drug approved by the FDA to treat patients following an overdose of 5-fluorouracil (5-FU) or capecitabine or in patients exhibiting early-onset, severe or life-threatening toxicity affecting the cardiac or central nervous system, and/or early-onset, unusually severe adverse reactions (e.g., gastrointestinal...
toxicity and/or neutropenia) within 96 hours following the end of 5-FU or capecitabine administration. VISTOGARD received orphan drug designation from the FDA as an antidote in the treatment of 5-FU poisoning and from the European Medicines Agency (EMA) as a treatment for 5-FU overdose. In Europe, under a named patient program, VISTOGARD is currently provided to patients at risk of excess 5-FU toxicity due to overdose and patients exhibiting severe toxicities to 5-FU within 96 hours of 5-FU administration.

For more information please visit www.vistogard.com.

About 5-Fluorouracil (5-FU)

5-FU is on the World Health Organization’s List of Essential Medicines, a compilation of the most important medications needed in a basic health system. Because 5-FU is administered in different doses and schedules as a frequent component of standard chemotherapy regimens for a variety of cancers, patients can experience dramatically different patterns of toxicity.

Used in combination with other chemotherapy agents and/or radiation, 5-FU has been for decades a mainstay of various treatment regimens for solid tumors, including those of the colon, pancreas, stomach, esophagus, breast, and head and neck. The drug is most commonly administered by infusion pump at or near what is considered the maximum tolerated dose. Expected side effects of 5-FU include myelosuppression (a reduction in white-blood-cell counts and thus increased risk of infection), diarrhea, nausea, vomiting, and mucositis (a painful inflammation and ulceration of the mucous membranes lining the digestive tract). Overexposure to 5-FU can lead to severe myelosuppression, gastrointestinal hemorrhage, septic shock, multiple organ failure, cardiac and neurological complications and death.

About Capecitabine

Capecitabine is a fluoropyrimidine carbamate with antineoplastic activity. It is an orally administered systemic prodrug of 5'-deoxy-5-fluorouridine (5'-DFUR) which is converted after administration to 5-fluorouracil.

About Wellstat Therapeutics

Wellstat Therapeutics Corporation is a privately-held biopharmaceutical company located in Gaithersburg, Maryland. Wellstat Therapeutics is committed to discovering, developing and commercializing products that will provide new and improved treatments for patients in the fields of oncology and metabolic, neurometabolic and neurodegenerative diseases. For more
About BTG

BTG is a growing international specialist healthcare company bringing to market innovative products in specialist areas of medicine to better serve doctors and their patients. We have a portfolio of Interventional Medicine products to advance the treatment of liver tumors, advanced emphysema, severe blood clots and varicose veins, and Specialty Pharmaceuticals that help patients overexposed to certain medications or toxins. Inspired by patient and physician needs, BTG is investing to expand its portfolio to address some of today’s most complex healthcare challenges. To learn more about BTG, please visit: www.btgplc.com.

# # #