Synta Announces First Patient Treated in Phase 1 Trial of Elesclomol in Acute Myeloid Leukemia

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LEXINGTON, Mass., Feb 08, 2011 (BUSINESS WIRE) -- Synta Pharmaceuticals Corp. (NASDAQ: SNTA), a biopharmaceutical company focused on discovering, developing, and commercializing small molecule drugs to treat severe medical conditions, today announced that the first patient has been treated in a Phase 1 single agent trial of elesclomol in acute myeloid leukemia (AML). Elesclomol is a first-in-class investigational drug candidate that triggers programmed cell death (apoptosis) in cancer cells through a novel mechanism: targeting mitochondrial energy production in cancer cells. The trial is being conducted at Princess Margaret Hospital in Toronto, Canada and at Memorial Sloan-Kettering Cancer Center in New York.

"Results presented at the 2009 Annual Meeting of the American Society for Hematology (ASH) demonstrated that all 10 samples of primary AML blast cells from patients in an *ex vivo* study responded to exposure to elesclomol," said Aaron Schimmer, M.D., F.R.C.P.C., Ph.D., Ontario Cancer Institute, and Department of Medical Oncology, Princess Margaret Hospital, Toronto and principal investigator on the trial. "These results as well as its novel mechanism of action provide a strong rationale for studying elesclomol as a single agent for the treatment of relapsed and refractory AML, a disease for which there is an urgent need for new agents."

"Elesclomol has a novel and exciting mechanism of action: targeting cancer cell energy metabolism," said Vojo Vukovic, M.D., Ph.D., Senior Vice President and Chief Medical Officer, Synta Pharmaceuticals. "Elesclomol in combination with paclitaxel-based chemotherapy has shown potential for clinical benefit in patients with low lactate dehydrogenase (LDH) levels in three randomized clinical trials. We believe that the unique mechanism of action and identification of a predictive biomarker provide a new approach, entirely distinct from conventional chemotherapy or kinase inhibition, to treating a broad range of hematologic and solid tumor cancers."

Study Design

This trial will enroll up to 36 patients with relapsed or refractory AML and total baseline serum LDH level less-than or equal to 0.8 upper limit of normal (ULN). Patients will be treated with elesclomol sodium on a once-weekly schedule at a starting dose of 200 mg/m^2, with dose escalation planned based on safety and tolerability. The primary endpoints are to characterize the safety and tolerability of elesclomol sodium and to determine the pharmacokinetics of elesclomol and its metabolites in this patient population. Secondary endpoints include assessing the activity of elesclomol as a monotherapy in the treatment of AML.

About Elesclomol

Elesclomol is a first-in-class, investigational drug candidate that triggers programmed cell death

(apoptosis) in cancer cells through a novel mechanism: selectively targeting the electron transport chain in cancer cell mitochondria, disrupting cancer cell energy metabolism.

Elesclomol binds copper in plasma, which causes a change in conformation that enables its uptake through membranes and into cells. Elesclomol binds copper in an oxidative, positively charged, state called Cu(II). Once inside mitochondria, an interaction with the electron transport chain reduces the copper from Cu(II) to Cu(I), resulting in a cascade of redox reactions, a rapid increase of oxidative stress, disruption of mitochondrial energy production, and the initiation of the mitochondrial apoptosis pathway.

Mitochondria generate energy for cells, but also can induce apoptosis under certain conditions, such as a high level of oxidative stress. By sensitizing mitochondria and reducing barriers to apoptosis, elesclomol may provide a means to overcome resistance to traditional chemotherapy or targeted therapy.

Cancer cell mitochondria can be selectively targeted by elesclomol because cancer cell mitochondria are structurally and functionally different from their normal counterparts, making them more susceptible to changes to mitochondrial metabolism.

About Elesclomol and LDH

Lactate dehydrogenase (LDH) is an enzyme that plays a key role in cancer cell energy metabolism. Under normal oxygen (normoxic) conditions, energy in tumors is primarily generated by conversion of nutrients to ATP in the mitochondria, with oxygen as a key component of this process. Levels of LDH generally remain in the normal range in this state. Under low oxygen (hypoxic) conditions, energy in tumors is primarily generated by glycolysis in the cytoplasm, and levels of LDH increase.

Elesclomol has been shown to have potent anti-cancer activity in a broad range of cancer types under normoxic conditions. Under hypoxic conditions, elesclomol's ability to disrupt oxygen-mediated energy production has limited effect, and elesclomol loses anti-cancer activity.

Clinical observations have been consistent with the preclinical findings that elesclomol activity depends on metabolic state. In three randomized trials, in a total of over 800 patients, elesclomol showed clinical activity that correlated with baseline level of LDH. Benefit was seen only in patients with the low to normal levels of LDH that are associated with normoxic conditions. The most common adverse events in the elesclomol plus paclitaxel group included fatigue, alopecia, constipation, nausea, hypoaesthesia, arthralgia, insomnia, diarrhea, and anemia.

About Acute Myeloid Leukemia

Acute myeloid leukemia (AML) is a cancer that starts inside bone marrow, the soft tissue inside bones that helps form blood cells. The cancer grows from cells that would normally turn into white blood cells. According to the American Cancer Society, in 2010 12,330 Americans were diagnosed with AML and 8,950 were expected to die from the disease.

About Synta Pharmaceuticals

Synta Pharmaceuticals Corp. is a biopharmaceutical company focused on discovering, developing, and commercializing small molecule drugs to extend and enhance the lives of patients with severe medical conditions, including cancer and chronic inflammatory diseases. Synta has a unique

chemical compound library, an integrated discovery engine, and a diverse pipeline of clinical- and preclinical-stage drug candidates with distinct mechanisms of action and novel chemical structures. All Synta drug candidates were invented by Synta scientists using our compound library and discovery capabilities. For more information, please visit www.syntapharma.com.

Safe Harbor Statement

This media release may contain forward-looking statements about Synta Pharmaceuticals Corp. Such forward-looking statements can be identified by the use of forward-looking terminology such as "will", "would", "should", "expects", "anticipates", "intends", "plans", "believes", "may", "estimates", "predicts", "projects", or similar expressions intended to identify forward-looking statements. Such statements, including statements relating to the timing, developments and progress of our clinical and preclinical programs, reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such forward-looking statements, including those described in "Risk Factors" of our Form 10-K for the year ended December 31, 2009 as filed with the Securities and Exchange Commission. Synta undertakes no obligation to publicly update forward-looking statements, whether because of new information, future events or otherwise, except as required by law.

SOURCE: Synta Pharmaceuticals Corp.

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