Synta Pharmaceuticals Announces First Patient Treated in Elesclomol Monotherapy Solid Tumor Clinical Study

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LEXINGTON, Mass.--(BUSINESS WIRE)--Feb. 10, 2009-- Synta Pharmaceuticals Corp. (NASDAQ: SNTA), a biopharmaceutical company focused on discovering, developing, and commercializing small molecule drugs to treat severe medical conditions, today announced the first patient has been treated in a single agent, dose escalation clinical study of its novel oxidative stress inducer, elesclomol, in solid tumors.

Elesclomol is a first-in-class investigational drug, believed to work by exploiting a fundamental vulnerability of many cancer cells – their elevated level of reactive oxygen species (ROS) and diminished anti-oxidant capacity. By further elevating ROS levels in cancer cells, elesclomol increases oxidative stress, triggering programmed cell death (apoptosis) while leaving normal cells relatively unaffected. Elesclomol is not approved for marketing by any regulatory body in any country.

"This is the first clinical trial that will study the potential anti-cancer activity of elesclomol as a single agent," said Eric Jacobson, M.D., Senior Vice President and Chief Medical Officer, Synta. "In addition, this trial will allow us to further evaluate the safety and tolerability of elesclomol in solid tumors."

The open-label, dose-escalation study of elesclomol in up to 30 subjects with advanced metastatic or unresectable solid tumors is designed to identify the maximum tolerated dose of elesclomol sodium based on a weekly infusion dosing schedule. Pharmacokinetic, safety and efficacy endpoints, including tumor response and durability of response will also be evaluated. This study uses a water soluble (sodium salt) formulation, allowing flexible administration, either as monotherapy or in combination with other anti-cancer agents.

About Elesclomol

Elesclomol is a novel, injectable, investigational drug candidate that triggers apoptosis (programmed cell death) in cancer cells. Cancer cells operate at high levels of reactive oxygen species, or oxidative stress. Elesclomol is believed to act by increasing the level of oxidative stress in cancer cells even further, beyond sustainable levels, inducing apoptosis. This mechanism of action, called oxidative stress induction, represents a novel way of selectively targeting and killing cancer cells.

In a double-blind, randomized, controlled Phase 2b clinical trial in 81 patients with stage IV metastatic melanoma, elesclomol in combination with paclitaxel met the primary endpoint, doubling the median time patients survived without their disease progressing, compared to paclitaxel alone ($p = 0.035$). The most common adverse events in the elesclomol plus paclitaxel group seen in at least 20% of patients included fatigue, alopecia, constipation, nausea, hypoaesthesia, arthralgia,

insomnia, diarrhea, and anemia.

Ongoing Clinical Trials

A global, pivotal Phase 3 clinical trial of elesclomol in combination with paclitaxel in patients with stage IV metastatic melanoma (the SYMMETRY trial) has completed enrollment. Elesclomol is also being studied in an open-label Phase 1/2 study of elesclomol in combination with docetaxel in approximately 34 patients with advanced metastatic, hormone refractory prostate cancer. Additional trials to evaluate elesclomol as a therapy for other cancers are planned.

About Oxidative Stress

Oxidative stress in cells is the presence of elevated levels of reactive oxygen species (ROS) such as oxygen radicals and hydrogen peroxide. ROS can be generated by many processes and stimuli, including ordinary cell metabolism, exposure to heat or radiation, or attack by bacteria or viruses. Because ROS can react chemically with different proteins and other elements of a cell, altering their normal function, prolonged exposure to elevated levels of ROS can cause serious damage to a cell. To protect against this damage, cells have natural defense mechanisms – anti-oxidant abilities – to clear excessive levels of ROS and to repair the disruption they cause.

Normal, non-cancer cells typically function at a low, steady-state level of oxidative stress. Their strong anti-oxidant capacity guards against prolonged, excessive levels of ROS. Cancer cells, however, typically operate at a much higher level of oxidative stress than normal cells, and have a greatly diminished anti-oxidant capacity. This diminished capacity to clear ROS leaves them vulnerable to further increases in oxidative stress. In particular, when ROS levels exceed a natural breaking point, continued survival of the cell becomes unsustainable. At levels of ROS above this breaking point, a switch inside the mitochondria is triggered that causes the cell to initiate programmed cell death, also known as apoptosis.

By elevating ROS, an oxidative stress inducer such as elesclomol exploits this difference between cancer cells and normal cells. Elesclomol has been observed to have little to no effect *in vitro* on most normal cells. In contrast, elesclomol has been observed to potently induce apoptosis in cancer cells. In preclinical models elesclomol showed potent anti-cancer activity against a broad range of cancer cell types, as well as an ability to enhance the efficacy of certain chemotherapy agents with minimal additional toxicity.

Oxidative stress induction represents a novel approach to treating cancer. It is distinct from chemotherapy, from "targeted" agents such as kinase inhibitors and antibodies, and from angiogenesis inhibitors in that OS inducers exploit a fundamentally different vulnerability of cancer cells – the elevated levels of reactive oxygen species.

For more on oxidative stress and cancer see for example J. Fruehauf et al, Clin Cancer Res 2007;13 (3) and references therein; for more on oxidative stress in melanoma see for example H. Wittgen et al, Melanoma Research 2007;17 (400) and references therein.

Collaboration with GlaxoSmithKline

In October 2007, Synta and GSK entered into a collaboration agreement for elesclomol. Under the terms of the agreement, the companies will jointly develop and commercialize elesclomol in the U.S. and GSK will have exclusive responsibility for development and commercialization of elesclomol

outside the U.S. Synta is responsible for the Phase 3 melanoma study and the filing of the New Drug Application with the FDA.

Synta and GSK are working closely together to further the clinical development of elesclomol as well as prepare for the manufacture and commercial launch of elesclomol.

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 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, 2007 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.

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