Synta Presents Results Showing Elesclomol Selectivity in Targeting Cancer Cell Metabolism

November 16, 2011

LEXINGTON, Mass.--(BUSINESS WIRE)--Nov. 16, 2011-- Synta Pharmaceuticals Corp. (NASDAQ: SNTA), today presented results at the AACR-EORTC-NCI Molecular Targets and Cancer Therapeutics Conference showing that elesclomol activity is selective for cancer cells and that continuous, low level infusion of elesclomol demonstrates single agent anti-cancer activity.

Elesclomol is a first-in-class mitochondrial metabolism inhibitor that exerts potent anti-cancer activity through targeting the electron transport chain in mitochondria. Elesclomol is currently being studied as a single agent in a Phase 1 trial in acute myeloid leukemia and a Phase 2 trial in combination with paclitaxel in ovarian cancer sponsored by the Gynecological Oncology Group.

“In three randomized trials, once-weekly dosing of elesclomol in combination with paclitaxel has demonstrated clear evidence of activity in patients with low lactate dehydrogenase (LDH),” said Vojo Vukovic, M.D., Ph.D, Chief Medical Officer, Synta. “The *in vivo* results presented today show that continuous low level infusion of elesclomol achieved sustained levels of the active elesclomol-copper complex and demonstrated single agent anti-cancer activity in several human tumor xenograft models. Importantly, this new schedule of elesclomol administration showed good tolerability and a favorable toxicity profile.”

In vitro results demonstrated that elesclomol causes specific and preferential accumulation of copper in cancer cell mitochondria, thereby increasing levels of mitochondrial reactive oxygen species (ROS) in tumor cells ultimately leading to apoptosis (programmed cell death). In contrast, treatment with elesclomol did not result in copper accumulation or apoptosis in normal blood cells.

“Our improved understanding of the mechanism of action of elesclomol and identification of biomarkers for selection of patients that are most likely to benefit from elesclomol treatment suggests potentially wide application in a range of human cancers. Today’s presentation points to a path forward in clinical development of elesclomol both as a single agent as well as in combination with other anti-cancer agents,” concluded Dr. Vukovic.

Continuous elesclomol infusion results in enhanced single agent antitumor efficacy

Poster Presentation: November 15, 3:30 p.m. ET
Title: *Cancer-selective mitochondrial copper transport by elesclomol results in potent single agent efficacy in multiple tumor types.*
Permanent Abstract Number: C168

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 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.

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Source: Synta Pharmaceuticals Corp.

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