Synta Announces Gynecologic Oncology Group (GOG) to Initiate Phase 2 Clinical Trial of Elesclomol for the Treatment of Ovarian Cancer

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NCI-CTEP funding of $300K to support clinical trial

LEXINGTON, Mass., Nov 01, 2010 (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 Gynecologic Oncology Group (GOG) will initiate a Phase 2 clinical trial of elesclomol in combination with paclitaxel for the treatment of persistent or recurrent ovarian, fallopian tube or primary peritoneal cancer. The GOG is a non-profit organization with the purpose of promoting excellence in the quality and integrity of clinical and basic scientific research in the field of gynecologic malignancies.

Synta also announced that the National Cancer Institute (NCI) will provide financial support of up to approximately $300,000 for the trial through its Cancer Therapy Evaluation Program (CTEP).

"There are few treatment options for women whose cancer has progressed after first and second line treatment with approved agents including platinum-based therapies," said Bradley J. Monk, M.D., Department of Obstetrics and Gynecology, Creighton University School of Medicine at St. Joseph's Hospital and Medical Center and the principal investigator on the trial. "Based on the synergistic anti-tumor activity seen in a number of preclinical models as well as encouraging activity seen in an ovarian cancer patient in a Phase 1 study of elesclomol, we believe that the combination of elesclomol and paclitaxel holds promise in patients with low baseline levels of lactate dehydrogenase (LDH) in this difficult-to-treat form of ovarian cancer."

"Elesclomol in combination with paclitaxel-based chemotherapy has shown potential for clinical benefit in patients with low to normal LDH levels in three randomized clinical trials: Phase 2b and Phase 3 trials in metastatic melanoma and a Phase 2b trial in non-small cell lung cancer," said Vojo Vukovic, M.D., Ph.D., Senior Vice President and Chief Medical Officer, Synta Pharmaceuticals. "By directly targeting cancer cell energy metabolism - which represents a novel mechanism, distinct from chemotherapy or kinase inhibition - and with the benefit of a predictive biomarker to help select the patients most likely to respond, elesclomol has the potential to be an exciting, new approach to treating ovarian cancer and other malignancies."

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 (ETC) 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 the Phase 2 Ovarian Cancer Clinical Trial

The Phase 2 single-arm, open-label study will recruit up to approximately 50 patients who have progressed on platinum-based therapy. Eligible patients are allowed to have received an additional non-cytotoxic regimen but may not have received additional cytotoxic therapy. The primary objectives of the trial are to assess activity, based on objective response rate, and safety of the combination in this patient population. Secondary objectives include progression-free survival and overall survival. Elesclomol sodium 200 mg/m^2 and paclitaxel 80 mg/m^2 will be given as separate 1 hour IV infusions weekly for three weeks followed by one week rest, comprising a four-week cycle. Treatment may continue until disease progression.

About Ovarian Cancer

According to the American Cancer Society approximately 21,880 new cases of ovarian cancer will be diagnosed in the United States in 2010 and about 13,850 women will die from the disease.

Ovarian cancer is the ninth most common cancer among women, excluding non-melanoma skin

cancers. It ranks fifth in cancer deaths among women, accounting for more deaths than any other cancer of the female reproductive system. Ovarian cancer accounts for about 3% of all cancers in women. About 3 in 4 women with ovarian cancer survive at least 1 year after diagnosis. The five year survival rate for women with ovarian cancer is 46%. If ovarian cancer is found (and treated) before the cancer has spread outside the ovary, the 5-year survival rate is 93%. However, less than 20% of all ovarian cancer is found at this early stage.

References:

Markman M, Blessing J, Rubin SC, Connor J, Hanjani P, Waggoner S. Phase II trial of weekly paclitaxel (80 mg/m2) in platinum and paclitaxel-resistant ovarian and primary peritoneal cancers: A Gynecologic Oncology Group study. Gynecol Oncol 101:436-440, 2006.

O'Day, S., et.al.: A Phase II, Randomized, Controlled, Double-Blinded Trial of Weekly Elesclomol Plus Paclitaxel Versus Paclitaxel Alone for Stage IV Metastatic Melanoma. J Clin Oncol. 2009 Oct 13.

ASCO Annual Meeting 2010, June 6, 2010 -Phase III, randomized, double-blind study of elesclomol and paclitaxel versus paclitaxel alone in stage IV metastatic melanoma (MM): 1-year OS update.

ASCO Annual Meeting 2009, May 30, 2009 - Phase 3, randomized, double-blind study of elesclomol and paclitaxel versus paclitaxel alone in Stage IV metastatic melanoma

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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