Synta Reaches Agreement on Special Protocol Assessment and Initiates SYMMETRY Trial - a Pivotal Phase 3 Clinical Trial of Elesclomol in Metastatic Melanoma

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LEXINGTON, Mass.--(BUSINESS WIRE)--Nov. 12, 2007--Synta Pharmaceuticals Corp. (NASDAQ: SNTA) announced today that the first patients have been treated in the SYMMETRY(SM) trial - Synta Metastatic Melanoma Elesclomol Trial - a global, pivotal Phase 3 clinical trial to evaluate the safety and efficacy of elesclomol (formerly STA-4783) in patients with stage IV metastatic melanoma. Synta also reported that it has successfully completed the Special Protocol Assessment (SPA) process, reaching agreement with the FDA on the design, conduct, and planned analyses of the trial.

Elesclomol is a novel, small molecule, first-in-class drug candidate, discovered and developed by Synta, that acts by elevating the level of oxidative stress of cancer cells beyond a breaking point, inducing programmed cell death. In a recently completed Phase 2b double-blind, randomized, 21-center clinical trial in metastatic melanoma, treatment with elesclomol doubled median progression-free survival - the time patients survived without worsening of disease - achieving the primary endpoint of the study to statistical significance. In November 2006, Synta received Fast Track designation from the FDA for the development of elesclomol in metastatic melanoma. In October 2007, Synta announced a partnership with GlaxoSmithKline (GSK) to jointly develop and commercialize elesclomol.

"Metastatic melanoma is a devastating disease with a median survival of six to nine months and no improvement in standard of care in over 30 years," said Safi Bahcall, Ph.D., President and CEO, Synta. "Initiating the SYMMETRY trial is an important step in confirming the benefit to patients observed in our Phase 2b trial and creating a new treatment option for this disease."

"While melanoma has proven resistant to many traditional anti-cancer mechanism categories, we believe this type of cancer, which operates at a particularly high level of oxidative stress, may be especially vulnerable to the mechanism of action of elesclomol," said Eric Jacobson, M.D., Chief Medical Officer, Synta. "Because of the potential of this new approach and because there has never been a Phase 3 trial for a new agent in melanoma that has been preceded by a positive blinded, randomized study for the same agent, we are excited to initiate this trial and have been encouraged by the high level of interest from investigators. With approximately 630 patients and a design mirroring the prior trial, the SYMMETRY trial is highly powered to confirm the results from our Phase 2b trial and collect important additional information."

"The positive and constructive discussions with the FDA during the SPA process were important in providing us with clear guidance regarding critical aspects of our trial, and give us confidence the design of the program is suitable to support regulatory approval," continued Dr. Jacobson.

The Special Protocol Assessment process provides for a written agreement between the trial's sponsor and the FDA that the design and planned analyses of the clinical trial can be used in support of regulatory approval. For more information about the Special Protocol Assessment process, see http://www.fda.gov/cder/guidance/3764fnl.htm.

SYMMETRY Trial Design

The SYMMETRY trial is enrolling patients with stage IV metastatic melanoma who have not received prior chemotherapy but who may have already been treated with non-chemotherapeutic agents such as biologics. Approximately 630 patients will be enrolled in the blinded, randomized, controlled study, which will be conducted at approximately 150 centers worldwide. Patients will be randomized (1:1) to elesclomol (213 mg/m(2)) plus paclitaxel (80 mg/m(2)) or paclitaxel alone (80 mg/m(2)) and will receive three weekly treatments and one week without treatment per each four week cycle. If tolerated, treatment will continue until disease progression. Patients will be stratified according to LDH levels, M-grade status and prior treatment history. Responses will be assessed using standard RECIST criteria at baseline and at a minimum every other cycle, with radiology scans being assessed by independent, blinded, reviewers at a central site.

The control arm treatment, the combination arm treatment, the doses, the schedule, and the primary endpoint - progression free survival (PFS) - are the same as in the prior Phase 2b trial. This trial increases the total patient size from the prior trial and includes central review of radiology scans, stratification to ensure balance between treatment arms, and a no-crossover design for facilitating the assessment of overall survival.

There are two planned analyses for the primary endpoint, PFS:

-- An interim analysis to assess safety and non-futility will be conducted and reviewed by an independent, Data Safety Monitoring Board.

-- The final analysis for PFS will be initiated when enrollment is close to completion. At the time of the final analysis for PFS, a first interim analysis will also be performed for overall survival (OS), a secondary endpoint.

Following these, two additional analyses for OS are planned: a second interim analysis and a third and final OS analysis.

With 630 patients, the SYMMETRY trial is over 95% powered to detect a statistically significant improvement in PFS. Secondary endpoints in addition to overall survival include response rate, clinical benefit rate (defined as complete response, partial response, or stable disease at 24 weeks), and duration of response. Projections and powering assumptions are based on detecting an improvement of two months in PFS (67%, hazard ratio 0.60), or three months in OS (33%, hazard ratio 0.75).

Based on our current enrollment and event rate projections, Synta expects to complete the primary endpoint analysis by the end of 2008 and file a New Drug Application (NDA) with the Food and Drug Administration (FDA) by the first half of 2009.

The SYMMETRY trial is now open for patient recruitment. For those interested in more information

about the trial, please visit centerwatch.com/SYMMETRY or visit the Synta Pharmaceuticals website at: www.syntapharma.com.

Elesclomol Phase 2b Clinical Trial Results

The double-blind, randomized Phase 2b clinical trial was conducted in 21 centers in the United States and compared stage IV metastatic melanoma patients treated with elesclomol plus paclitaxel (N=53) vs. patients treated with paclitaxel alone (N=28). In the Phase 2b trial, patients who received elesclomol plus paclitaxel showed a doubling of median progression free survival (PFS), the primary endpoint of the study, compared to those patients who received paclitaxel alone (3.68 months vs. 1.84 months). This difference achieved statistical significance: p=0.035. In addition, the percentage of patients in the combination arm that were free of disease progression at six months more than doubled (35% vs. 15%), and the response rate more than tripled (15% vs. 4%).

In June 2007, at the American Society of Clinical Oncology (ASCO) annual meeting, Synta reported additional overall survival results from the Phase 2b trial. The analysis of overall survival showed that patients randomized to receive elesclomol plus paclitaxel (N=53) experienced a median survival of 12 months, compared to 7.8 months for all patients who initially received paclitaxel alone (N=28).

Elesclomol was generally well-tolerated in this study; side effects were predictable and were generally comparable to treatment with paclitaxel alone. Neutropenia occurred more commonly in the elesclomol plus paclitaxel group compared to the paclitaxel alone group, but this was manageable and reversible. Although paresthesias occurred more commonly in the elesclomol plus paclitaxel group, the incidence of severe events of this type was low and comparable between groups. The most common adverse events in the elesclomol plus paclitaxel group included fatigue, alopecia, constipation, nausea, hypoaesthesia, arthralgia, insomnia, diarrhea, and anemia.

About Metastatic Melanoma

Melanoma, the most deadly form of skin cancer, arises from melanocytes, the pigment-producing cells of the skin. According to the American Cancer Society, melanoma accounts for approximately five percent of all skin cancers but causes about 75% of all skin cancer-related deaths. An estimated 60,000 people will be diagnosed and nearly 8,200 people will die from melanoma this year in the U.S. alone. If diagnosed and surgically removed while localized in the outermost skin layer, melanoma is potentially curable; however, for patients with metastatic disease, the prognosis is poor, with limited available treatments and an expected survival of only six to nine months. The incidence of melanoma has increased more rapidly than any other cancer during the past ten years. The FDA has not approved a novel, small molecule drug for the treatment of metastatic melanoma in over 30 years.

About Oxidative Stress and Apoptosis

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 stimuli, including ordinary cell metabolism, exposure to heat or radiation, or attack by bacteria or viruses. Normal cells have a strong anti-oxidant capacity that regulates the 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. When ROS levels exceed a critical threshold, continued survival of the

cell becomes unsustainable and programmed cell death (apoptosis) is initiated.

In a series of in vitro and in vivo experiments, elesclomol has been shown to rapidly cause a dramatic increase in the level of ROS inside cancer cells and induce apoptosis. At similar doses and exposure, elesclomol has little to no impact on non-cancer cells. The high selectivity for targeting cancer cells may explain the favorable safety profile observed in preclinical experiments, including a therapeutic index - the ratio of maximum tolerated dose to efficacious dose - significantly higher than many commonly-used chemotherapies.

Elevated oxidative stress induces apoptosis through the mitochondrial pathway. In addition to potent induction of oxidative stress and apoptosis in cancer cells as a single agent, elesclomol has been shown to enhance the activity of other anti-cancer agents that act through the mitochondrial pathway. These include commonly used first line agents such as paclitaxel, docetaxel, gemcitabine, and rituximab.

Oxidative stress induction represents a novel anti-cancer strategy - a novel way of differentiating, and selectively killing, cancer cells vs. normal cells.

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. Synta has a partnership with GlaxoSmithKline for the joint development and commercialization of its lead investigational drug candidate, elesclomol, which is in a pivotal Phase 3 clinical trial for the treatment of metastatic melanoma. 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, 2006 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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