



## **Synta Completes Enrollment of the Phase 3 SYMMETRYSM Trial of Elesclomol in Stage IV Metastatic Melanoma**

February 2, 2009

**Primary endpoint results expected 1H 2009**

LEXINGTON, Mass.--(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 it met its target of 630 patients for the SYMMETRY<sup>SM</sup> trial - a global, pivotal Phase 3 clinical trial to evaluate the efficacy and safety of elesclomol in patients with stage IV metastatic melanoma.

"We are tremendously grateful to the hundreds of patients who have elected to participate in the SYMMETRY trial as well as the physicians and other healthcare professionals at over 150 sites in 15 countries who have been and continue to be so critical to the successful completion of this pivotal trial," said Dr. Eric Jacobson, Chief Medical Officer. "Metastatic melanoma is a devastating disease which affects tens of thousands of people each year. We are hopeful this trial will advance our understanding of the role oxidative stress induction may play in the treatment of melanoma."

"Today's milestone represents a terrific achievement on the part of the full SYMMETRY team – the Synta employees, physicians, nurses, healthcare professionals and our partners around the world who came together to enroll one of the largest pivotal trials for a new agent in this disease so rapidly and effectively," said Dr. Safi Bahcall, President and CEO. "The speed, the quality, and the professionalism with which this trial was conducted show what a highly motivated team can accomplish when given an ambitious goal and an urgent medical need. We intend to conduct the primary endpoint analysis with the same attention to detail and high standards of excellence; our goal is to complete this analysis by May of this year. We are hopeful that this effort on the part of so many will translate into a new therapy for patients."

Elesclomol is being developed under a global collaboration agreement between Synta Pharmaceuticals and GlaxoSmithKline and is not approved for marketing by the U.S. Food and Drug Administration (FDA) or any other similar regulatory body in any country.

### **About Elesclomol**

Elesclomol is an investigational first-in-class oxidative stress inducer that triggers apoptosis (programmed cell death) in cancer cells. Cancer cells operate at high levels of reactive oxygen species, or oxidative stress. Elesclomol acts 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 included fatigue, alopecia, constipation, nausea, hypoaesthesia, arthralgia, insomnia, diarrhea, and anemia.

A pivotal Phase 3 clinical trial of elesclomol in combination with paclitaxel in patients with stage IV metastatic melanoma (the SYMMETRY trial) has completed enrollment; a Phase 1/2 trial in hormone-refractory prostate cancer, in combination with docetaxel, is ongoing. Phase 2 trials in other indications, and in combination with other agents, are planned.

### **About the SYMMETRY Trial**

The SYMMETRY trial, a double-blind, randomized, controlled study conducted at approximately 150 centers worldwide, has enrolled patients with stage IV metastatic melanoma who had not received prior chemotherapy but who may have already been treated with non-chemotherapeutic agents such as biologics. Patients have been randomized (1:1) to elesclomol ( $213 \text{ mg/m}^2$ ) plus paclitaxel ( $80 \text{ mg/m}^2$ ) or paclitaxel alone ( $80 \text{ mg/m}^2$ ) and receive three weekly treatments followed by one week without treatment per each four week cycle. If tolerated, treatment continues until disease progression. The primary endpoint of the study is progression-free survival; overall survival and response rate are secondary endpoints. Progression and response are based on standard RECIST criteria, with scans assessed at a minimum of every eight weeks and independently reviewed at a central site.

The control arm treatment, the combination arm treatment, the doses, the schedule, and the primary endpoint are the same as in the prior Phase 2b trial. The SYMMETRY 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.

The Phase 3 SYMMETRY trial completed the Special Protocol Assessment process with the FDA and initiated enrollment in the Fall of 2007. Screening for new patients closed in January 2009. Peak enrollment achieved was 82 patients per month.

Elesclomol has received Fast Track and Orphan Drug designation from the FDA for metastatic melanoma.

### **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 Metastatic Melanoma**

Melanoma, the most deadly form of skin cancer, arises from melanocytes, the pigment producing

cells of the skin. The National Cancer Institute estimates that in 2008 62,480 people will be diagnosed with and 8,420 will die of melanoma in the United States alone. While melanoma accounts for approximately five percent of all skin cancers, it causes about 75% of all skin cancer-related deaths. If diagnosed and surgically removed while localized in the outermost skin layer, melanoma is potentially curable; however, for patients with deeper lesions or 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**

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.

## **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 has completed enrollment in a global, pivotal Phase 3 clinical trial for the treatment of metastatic melanoma. For more information, please visit [www.syntapharma.com](http://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 anticipated timing of the primary endpoint results for the SYMMETRY trial, 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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