Results Presented at AACR Differentiate STA-9090 in Hsp90 Inhibitor Class and Show Activity in Erlotinib (Tarceva(R))-resistant Lung Cancer Models

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Novel Synta Hsp90 inhibitor shows up to 100x greater potency and reduced toxicity relative to 17-AAG in both in vitro and in vivo models

STA-9090 shows activity in models resistant to 17-AAG

LEXINGTON, Mass.--(BUSINESS WIRE)--Apr. 21, 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 that preclinical data presented at the annual meeting of the American Association for Cancer Research (AACR) shows that STA-9090, a novel, synthetic inhibitor of heat shock protein 90 (Hsp90), demonstrated greater activity in lung cancer cells when compared to the 17-AAG class of Hsp90 inhibitors, the class most advanced in the clinic.

“The results presented today from the preclinical experiments performed at Dr. Geoffrey Shapiro’s lab at the Dana-Farber Cancer Institute provide compelling evidence that STA-9090 may have substantial and important advantages over the first generation of Hsp90 inhibitors, such as 17-AAG,” said Jim Barsoum Ph.D., Senior Vice President, Research, Synta Pharmaceuticals. “Inhibition of Hsp90 is an area of great interest in the oncology community because of the broad role played by Hsp90 in maintaining the function of many cancer-promoting proteins. The results presented today highlight the effectiveness of STA-9090 in lung cancer, including lung cancers resistant to Tarceva. This activity against cancers resistant to a kinase inhibitor is consistent with the underlying rationale of targeting the Hsp90 chaperone protein rather than the kinase itself. Along with work presented by Dr. Shapiro’s lab, we and our collaborators have shown broad activity of STA-9090 against multiple cancer types, including both cancers that are sensitive to kinase inhibitors, such as Gleevec and Sutent, and cancers that are resistant to those kinase inhibitors. These collective results have shown that STA-9090 is differentiated within the Hsp90 inhibitor class, including improved potency and reduced toxicity compared to the 17-AAG family of inhibitors.”

“In addition to our three on-going clinical trials of STA-9090, we are excited to advance this program in the clinic. We are pleased by the enthusiasm from the scientific and medical community for this program and plan to initiate trials in a range of new cancer types later this year,” continued Dr. Barsoum.

STA-9090 is an example of the ability of Synta to continue to generate novel, best-in-class drug candidates using its discovery platform and unique compound library of diverse, proprietary chemical structures. Synta has five drug candidate programs in preclinical or clinical development each representing distinct mechanisms of action, chemical structures, and market opportunities. All programs have been discovered and developed internally.

The Hsp90 data, presented in a poster by Takeshi Shimamura, Ph.D. and Geoffrey Shapiro, M.D., Ph.D., of the Dana-Farber Cancer Institute, showed that, depending on the experimental model, STA-9090 was up to 100 times more potent than the geldanamycin inhibitor 17-AAG in both *in vitro* and *in vivo* models in non-small cell (NSCLC).

Additional findings demonstrated that:

- STA-9090 inhibited proliferation and induced apoptosis in a large panel of NSCLC cell lines with a more than four–fold greater potency than 17-AAG.
- STA-9090 displayed activity against cell lines expressing seventeen different epidermal growth factor receptor (EGFR) mutations commonly found in NSCLC patients, including ten mutations that conferred resistance to the EGFR inhibitor erlotinib (Tarceva).
- STA-9090 induced depletion of Hsp90 clients such as AKT, EGFR, ERBB4, IGF-1R, c-MET, PDGFRα, and c-RET a 3 to 9-fold lower drug concentrations than for 17-AAG.
- STA-9090 retained activity against lung cancer cell lines that were resistant to treatment with 17-AAG.
- STA-9090 showed greater efficacy and an increased therapeutic index relative to 17-AAG in mouse models of Tarceva-resistant NSCLC.

It is estimated that 215,020 men and women (114,690 men and 100,330 women) in the United States were diagnosed with and 161,840 men and women died of cancer of the lung and bronchus in 2008[1].

STA-9090 is currently being studied in two Phase 1 solid tumor clinical trials and one Phase 1/2 trial in hematologic cancers. Synta has announced that a second Phase 2 hematologic cancer trial will be started in 2009.

Additional Abstracts Presented at AACR

Also presented at AACR was a poster by Xiaojiang Cui, Ph.D., of the John Wayne Cancer Institute, which concluded that combining elesclomol with the cytotoxic chemotherapeutic agents doxorubicin and paclitaxel induced apoptosis in breast cancer cells. Activation of c-Jun N-terminal kinase (JNK) signaling and downregulation of survival proteins appeared to play a role in the induction of apoptosis. In addition, Akt/Hsp70 survival signaling was also strongly induced by elesclomol. Blockade of Akt activation using a small molecule inhibitor enhanced elesclomol-elicited apoptosis.

About STA-9090

In preclinical studies, STA-9090 has shown the ability to inhibit multiple kinases with comparable potency to, and a broader activity profile than specific kinase inhibitors such as imatinib, erlotinib, and sunitinib. In addition, STA-9090 has shown potency 10 to 100 times greater than the ansamycin family of Hsp90 inhibitors such as 17-AAG, as well as activity against a wider range of kinases. In *in vivo* models, STA-9090 has shown strong efficacy in a wide range of cancer types, including cancers resistant to Gleevec and Tarceva.

About Hsp90

Hsp90 is an emerging therapeutic target of interest for the treatment of cancer. It is responsible for the maturation and function of numerous signaling proteins – known as ‘client proteins’ – that are

associated with cancer cell survival and proliferation. Many cancers result from specific mutations in, or aberrant expression of, these client proteins. Examples of cancer-associated client proteins of Hsp90 include c-KIT in gastrointestinal stromal tumors, epidermal growth factor receptor (EGFR) in lung cancer, and BCR-ABL in chronic myelogenous leukemia. In preclinical studies, inhibiting Hsp90 causes the degradation of these proteins and cancer cell death. Inhibiting Hsp90 has also proven effective in killing cancer cells that have developed resistance to targeted therapies such as kinase inhibitors.

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. Clinical trials of elesclomol are on hold pending further analysis of the full results of the Phase 3 (SYMMETRY) trial.

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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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, developments and progress of our clinical and preclinical programs, possible partnering and financing opportunities, and the sufficiency of our cash resources for two or more years, 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, 2008 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.

1. NCI SEER database, 2009 http://seer.cancer.gov/statfacts/html/lungb.html

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