Synta Presents Preclinical Data on Next Generation Hsp90 Inhibitor, STA-9090

November 18, 2009

- Broad anti-cancer activity as a single agent and in combination
- Strong potency against highly resistant cancers
- Superior profile to first generation Hsp90 inhibitors

LEXINGTON, Mass.--(BUSINESS WIRE)--Nov. 18, 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 AACR-NCI-EORTC Conference on Molecular Targets and Cancer Therapeutics shows that STA-9090, a novel, synthetic inhibitor of heat shock protein 90 (Hsp90), demonstrated strong activity in multiple tumor models, including lung cancer, gastrointestinal stromal tumors (GIST), prostate cancer, colon cancer, breast cancer, gastric cancer, pancreatic cancer, colon cancer, melanoma, acute myeloid leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia, B-cell lymphoma, and multiple myeloma. Potent activity was shown in cancers resistant to treatment with imatinib (Gleevec®), sunitinib (Sutent®), and erlotinib (Tarceva®), including models with genetic mutations known to make those cancers highly resistant to treatment, such as the BCR-ABL T315I mutation in leukemias, the EGFR T790M mutation in lung cancer, and the KIT Ex 11 V654A and D820A mutations in GIST. STA-9090 was also shown to have potency superior to 17-AAG, the first generation, ansamycin-family Hsp90 inhibitor, across multiple tumor models and gene mutation profiles. Other results important for considering future clinical development with STA-9090 were presented, including results showing that STA-9090 enhances the activity of the widely used cancer drug paclitaxel.

“Taken together, the preclinical results presented at this conference demonstrate the potency, safety and broad activity profile of STA-9090, both as a single agent and in combination,” said Vojo Vukovic, M.D., Ph.D., Chief Medical Officer, Synta Pharmaceuticals. “There is a great deal of interest in the oncology community in the Hsp90 inhibitor category. Based on the strong scientific results we and others have seen with STA-9090, the superior safety and activity profile compared to first generation Hsp90 inhibitors, the limited success of first generation Hsp90 inhibitors in the clinic, and the encouraging clinical results seen to date with STA-9090, we believe STA-9090 can be the first Hsp90 inhibitor to realize the true potential of this category.”

STA-9090 is currently in four Phase 1 and Phase 1/2 trials. Synta expects to report data from these studies and initiate new trials across multiple tumor types later this year and in the first half of 2010.

Three posters related to STA-9090 were presented at the Conference:

STA-9090 is 5-15 fold more potent than 17-AAG in Gleevec-resistant GIST

Poster Presentation November 17, 12:30 p.m. ET

Title: Hsp90 inhibitor STA-9090 potently suppresses heterogeneous KIT kinase-domain mutations responsible for gastrointestinal stromal tumor progression during imatinib therapy.
Permanent Abstract Number: B184

GIST is a rare cancer affecting the digestive tract or nearby structures within the abdomen. Approximately 5,000 new cases of GIST are diagnosed in the United States each year with few therapeutic options available beyond surgery and treatment with tyrosine kinase inhibitors such as Gleevec.[1]

“Metastases taken from gastrointestinal stromal tumor patients whose cancers had progressed after treatment with imatinib are remarkably heterogeneous, displaying as many as eight distinct imatinib-resistance mutations in the KIT oncoprotein in different metastases taken from a single patient," said Jonathan Fletcher, M.D., Brigham and Women's Hospital, Boston, MA, and lead author on the GIST study. "This heterogeneity poses a significant challenge for the treatment of imatinib-resistant GIST. However, in our studies, all of these resistance mutations were still highly sensitive to STA-9090, which was 5 to 15 fold more potent than 17-AAG. STA-9090 also retained activity against GIST cells that were resistant to 17-AAG. These results suggest that STA-9090 has the potential to have broad clinical activity against imatinib-resistant GIST.”

STA-9090 is effective in multiple cancer models both as a single agent and in combination with paclitaxel

Poster Presentation November 17, 12:30 p.m. ET
Title: *In vitro* and *in vivo* efficacy of the novel Hsp90 inhibitor STA-9090 and its synergy with paclitaxel.
Permanent Abstract Number: B199

In *in vitro* studies, STA-9090 demonstrated on average approximately 30-fold greater potency than 17-AAG in 60 solid and hematologic cancer cell lines. Importantly, STA-9090 maintained its potency in cell lines of cancers which were resistant to kinase inhibitors such as Tarceva and Gleevec. *In vivo* studies of STA-9090 demonstrated strong single agent activity in cancers such as non-small cell lung cancer, gastric carcinoma and melanoma and hematologic malignancies such as acute myeloid leukemia, B-cell lymphoma, chronic myeloid leukemia and multiple myeloma. Activity was demonstrated in models that are particularly resistant to treatment, such as leukemias with the BCR-ABL T315I mutation. STA-9090 also demonstrated both *in vitro* and *in vivo* synergy with paclitaxel, including lung cancer models that were resistant to Tarceva, with no evidence of drug-drug interactions between the two agents.

STA-9090 in lung cancer supports infrequent dosing

Poster Presentation November 18, 12:30 p.m. ET
Title: Pharmacodynamic analysis of the Hsp90 inhibitor STA-9090 in a lung cancer xenograft model supports an infrequent dosing schedule in the clinic.
Permanent Abstract Number: C91

Hsp90 inhibition induces rapid client protein degradation, cell cycle arrest and apoptosis, however it has been hypothesized that frequent drug dosing in the clinic may be required to achieve optimal efficacy.

In vitro exposure to STA-9090 for as little as 5 minutes, however, was found to induce long-lasting cell growth inhibition and death, suggesting that even brief drug exposure *in vivo* may be sufficient to affect tumor growth. Consistent with this, STA-9090 has shown very broad *in vivo* efficacy in mouse cancer models. In particular, in a lung cancer model STA-9090 was found to be significantly more efficacious than 17-AAG, and pharmacodynamic studies demonstrated that a single drug dose was able to inhibit tumor cell proliferation and increased cell death up to several days after a single drug dose. These effects were correlated with long-lasting decreases in important signaling proteins regulated by Hsp90, such as EGFR, HER2, MET and RAF1. The studies also show that STA-9090 accumulated preferentially in tumors, with a tumor half-life of 58 hours, versus a half-life of 3-5 hours in the normal liver, lung and plasma. These results suggest that an infrequent dosing schedule may be effective in the clinic. These preclinical data are further supported by early clinical results, where once-a-week single agent dosing in solid tumors has resulted in responses in patients who have failed multiple prior therapies as well as instances of prolonged stable disease and a favorable safety profile.

About Hsp90

Hsp90 is a protein that maintains the function of numerous signaling proteins – known as 'client proteins' – 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 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 tyrosine kinase inhibitors.

About STA-9090

In preclinical studies, STA-9090 has shown the ability to inhibit multiple tyrosine kinases with comparable potency to, and a broader activity profile than specific inhibitors such as Gleevec, Sutent, and Tarceva. In addition, STA-9090 has shown potency up 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, Sutent, Tarceva, and 17-AAG. STA-9090 is currently in four Phase 1 and Phase 1/2 trials. Synta expects to report data from these studies and initiate new trials across multiple tumor types later this year and in the first half of 2010.

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.

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, developments 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, 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.

References

1. GIST Support International 2009, http://www.gistsupport.org/for-new-patients/faqs.php

Source: Synta Pharmaceuticals Corp.

Synta Pharmaceuticals Corp.
Rob Kloppenburg, 781-541-7125