Synta Pharmaceuticals Initiates Phase 2 Clinical Trial of STA-9090 in Gastrointestinal Stromal Tumors (GIST) following failure of Gleevec® and Sutent®

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STA-9090 shows encouraging preclinical and clinical results in GIST

LEXINGTON, Mass., Dec 23, 2009 (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 is initiating a Phase 2 clinical study of STA-9090 in patients with advanced gastrointestinal stromal tumors (GIST). This is the sixth clinical study of STA-9090, a potent, synthetic, small molecule Hsp90 inhibitor with a novel chemical structure.

"Both imatinib (Gleevec) and sunitinib (Sutent) have proven very effective in helping patients with GIST to live longer; however, the majority of patients will eventually experience disease progression despite treatment with both of those molecularly targeted therapies," said George Demetri, M.D., Dana-Farber Cancer Institute. "Once those two standard drugs fail, patients have a poor prognosis and very limited treatment options. Hsp90 inhibition is a promising therapeutic approach for these patients because the mutated kinase proteins that are the cause of resistance to both Gleevec and Sutentdepend upon being chaperoned and protected by the function of Hsp90. STA-9090 can potently inhibit the Hsp90 function and disrupt the mutant signaling in multidrug-resistant GIST. Based on the preclinical and early clinical results seen to date, STA-9090 has the potential to unlock the true potential of Hsp90 as a therapeutic target in GIST."

Preclinical results related to STA-9090 in GIST were presented by Jonathan Fletcher, M.D., Brigham and Women's Hospital, at the AACR-NCI-EORTC Conference on Molecular Targets and Cancer Therapeutics in November 2009.

"We have shown that as many as eight different secondary KIT Gleevec-resistance mutations can occur in different metastases from a single GIST patient whose disease has progressed after treatment with Gleevec, which poses a significant challenge for treating drug-resistant GIST," said Dr. Fletcher. "Importantly, all of these different resistance mutations were still sensitive to STA-9090. In these studies, STA-9090 was also 5-15 fold more potent than 17-AAG, a first-generation, ansamycin-family Hsp90 inhibitor. Additionally, STA-9090 was active against GIST cells that were resistant to 17-AAG."

"We and our collaborators have been encouraged by the strong preclinical results for STA-9090 in GIST as well as early clinical results from our solid tumor Phase 1 trials, where STA-9090 has generated objective tumor responses and has been well-tolerated, with the most common adverse events, fatigue and gastrointestinal toxicities, being manageable and reversible," said Vojo Vukovic, M.D., Ph.D., Senior Vice President and Chief Medical Officer, Synta Pharmaceuticals. "A particularly encouraging observation was that a GIST patient on our once- weekly dosing Phase 1 solid tumor

study, who experienced disease progression while on multiple prior therapies, including Gleevec and Sutent, experienced substantial tumor shrinkage and stabilization of disease following treatment with STA-9090. We are looking forward to working closely with leading GIST investigators to evaluate the potential of STA-9090 to benefit patients with this disease."

Synta expects to report data from the ongoing Phase 1 and Phase 1/2 trials and initiate studies in multiple other cancer indications in the first half of 2010.

Study Design in GIST

The non-randomized, open-label, multi-center Phase 2 study is designed to characterize the efficacy and safety of STA-9090 in patients with metastatic or unresectable GIST following failure of systemic treatment with imatinib (Gleevec) and sunitinib (Sutent). The trial will enroll up to approximately 55 patients in a two-stage design. Patients will be stratified according to whether or not they have been exposed to other Hsp90 inhibitors, and STA-9090 will be administered as a single agent on a once-weekly intravenous dosing schedule. Patients tolerating STA-9090 may continue on treatment until disease progression. Patients will be assessed for clinical benefit rate per RECIST criteria. Other objectives of the trial are to assess the impact of treatment with STA-9090 on certain biomarkers and to characterize the safety of STA-9090 in this patient population.

About STA-9090

STA-9090 is a potent, synthetic, small-molecule Hsp90 inhibitor, with a chemical structure unrelated to the first-generation, ansamycin family of Hsp90 inhibitors (e.g., 17-AAG). In preclinical studies, STA-9090 has shown potency up to 100 times greater than the first-generation Hsp90 inhibitors as well as activity against a wider range of kinases. In *in vitro* and *in vivo* models, STA-9090 has shown potent activity against a wide range of cancer types, including lung, prostate, colon, breast, gastric, pancreatic, melanoma and certain hematologic cancers - as well as potent activity against cancers resistant to imatinib (Gleevec), sunitinib (Sutent), erlotinib (Tarceva), and dasatanib (Sprycel).

In addition to the study announced today in gastrointestinal stromal tumors, Synta is currently conducting a Phase 2 trial in non-small cell lung cancer (NSCLC), two Phase 1/2 clinical trials of STA-9090 in hematologic cancers and two Phase 1 trials studies of STA-9090 in solid tumor cancers. The most common side effects of STA-9090 observed to date have been fatigue and gastrointestinal toxicities, which were manageable and reversible.

About Hsp90

Hsp90 is a chaperone protein required for the proper folding and activation of other cellular proteins, particularly kinases. Many of these "client proteins" of Hsp90 - such as AKT, BCR-ABL, BRAF, KIT, MET, EGFR, FLT3, HER2, PDGFRA, VEGFR - have been shown to be critical to cancer cell growth, proliferation, and survival and are the targets of clinically validated cancer drugs. In preclinical studies, inhibiting Hsp90 causes the degradation of multiple client proteins and leads to cancer cell death. Because mutated kinases which no longer respond to treatment with kinase inhibitors remain dependent on Hsp90 for their activity, inhibiting Hsp90 offers the potential for treating cancers that have become resistant to targeted therapies such as kinase inhibitors.

About Gastrointestinal Stromal Tumors (GIST)

A gastrointestinal stromal tumor (GIST) is a type of cancer that occurs in the gastrointestinal (GI or digestive) tract, including the esophagus, stomach, gallbladder, liver, small intestine, colon, and rectum. The American Cancer Society estimates 4,500 to 6,000 GIST cases are diagnosed each year in the United States. Although these tumors can start anywhere in the GI tract, they occur most often in the stomach (50% to 70%) or the small intestine (20% to 30%).

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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