Synta Presents Results at AACR-IASLC Demonstrating Potent and Synergistic Activity of STA-9090 in NSCLC Cell Lines Including Mutated EGFR, HER2, and KRAS

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LEXINGTON, Mass., Jan 12, 2010 (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 preclinical results presented at the AACR-IASLC (American Academy of Cancer Research - International Association for the Study of Lung Cancer) Joint Conference based on work done at Synta and at the Dana-Farber Cancer Institute in Boston showed that STA-9090, a potent, synthetic inhibitor of heat shock protein 90 (Hsp90), demonstrated potent activity against 100% of all non-small cell lung cancer cell lines tested, including those with EGFR, HER2 or KRAS mutations including the EGFR T790 mutation that is present in roughly 50% of cases of erlotinib or gefitinib resistance.

Synta is currently enrolling patients in a Phase 2 single-arm, open-label, single-agent study of STA-9090 in patients with stage IIIB or IV non-small cell lung cancer, with patient cohorts defined by the genetic profile of their tumors.

STA-9090 potently inhibited cell proliferation in 24 out of 24 human NSCLC lines tested irrespective of EGFR, HER2 or KRAS mutational status. *In vivo*, STA-9090 stopped tumor growth in both Tarceva(R) (erlotinib)-sensitive and Tarceva-resistant NSCLC xenograft models. In addition, in a HER2 positive adenosquamous lung cancer study, 3 out of 4 animals treated with STA-9090 experienced partial responses as measured by MRI.

Analysis of protein expression showed that STA-9090 causes substantial down-regulation of client proteins relevant to lung cancer growth and proliferation including AKT, EGFR, MET, HER2, CDK4, and RAF1.

Results in the animal models also showed that STA-9090 preferentially accumulates in tumors, with the half-life in tumors 10-19 times longer than the half-life in normal tissues and plasma. Six days after dosing, the tumor concentration of STA-9090 remained 215-fold higher than the median *in vitro* concentration needed for killing 50% of cells (IC-50) against the panel of 24 human NSCLC lines.

In *in vitro* studies of combination activity, STA-9090 demonstrated synergy with paclitaxel and docetaxel. These anti-cancer agents are widely used in the treatment of advanced-stage NSCLC. *In vivo*, the combination of STA-9090 with paclitaxel displayed greater efficacy than either agent used alone without additional toxicity.

"Taken together, the *in vitro* and *in vivo* results presented at this conference demonstrate the potency, broad activity, and safety profile of STA-9090, both as a single agent and in combination with taxanes in NSCLC," said Vojo Vukovic, M.D., Ph.D., Chief Medical Officer, Synta Pharmaceuticals. "Based on the strong scientific results we and others have seen with STA-9090,

the improved safety and activity profile compared to first-generation Hsp90 inhibitors, and the encouraging early clinical results seen to date with STA-9090, we believe STA-9090 can be the first Hsp90 inhibitor to realize the true clinical potential of this drug class."

The results presented today were performed in collaboration with the laboratories of Geoffrey Shapiro, M.D., Ph.D. and Kwok-Kin Wong, M.D., Ph.D., of the Dana-Farber Cancer Institute in Boston.

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(R)), sunitinib (Sutent(R)), erlotinib (Tarceva(R)), and dasatanib (Sprycel(R)).

Synta is currently conducting Phase 2 trials in non-small cell lung cancer (NSCLC) and gastrointestinal stromal tumors (GIST), two Phase 1/2 clinical trials of STA-9090 in hematologic cancers and two Phase 1 trials of STA-9090 in solid tumor cancers. The most common adverse events observed to date have been fatigue and gastrointestinal toxicities, which were manageable and reversible. Information on clinical trials with STA-9090 can be found at www.clinicaltrials.gov.

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 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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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.

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