



Synta Presents STA-9090 Results at AACR Including Synergy with Avastin(R), Tarceva(R), and Taxanes; Downregulation of HIF-1a; Inhibition of JAK/STAT

April 19, 2010

- STA-9090 shows *in vitro* and *in vivo* synergy with standard of care lung cancer agents -
- STA-9090 penetrates hypoxic regions of tumors and inhibits HIF-1a expression -
- STA-9090 inhibits JAK/STAT pathway, linked to cancer cell growth -

LEXINGTON, Mass., Apr 19, 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 American Association for Cancer Research (AACR) 101st Annual Meeting show that STA-9090, a potent, synthetic inhibitor of heat shock protein 90 (Hsp90), demonstrates synergy with standard of care therapies such as Avastin in non-small cell lung cancer models; penetrates efficiently into hypoxic (low oxygen) regions of tumors; and inhibits both HIF-1a and JAK/STAT signaling, pathways that are critical to the survival and proliferation of certain cancer types.

"STA-9090 has demonstrated encouraging signs of single-agent activity in our Phase 1 and Phase 2 clinical trials, as well as a manageable safety profile," said Vojo Vukovic, M.D., Ph.D., Senior Vice President and Chief Medical Officer, Synta Pharmaceuticals. "Results presented today further support the potential for STA-9090 in treating a range of cancers, both as a single-agent and in combination with other anti-cancer agents."

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. Synta will present data from the Phase 1 solid tumor studies at ASCO 2010 and expects to initiate six to ten new trials across multiple tumor types later this year.

STA-9090 synergizes with standard of care therapies in NSCLC models

Poster Presentation April 19, 2:00 p.m. ET

Title: [Hsp90 inhibitor STA-9090 enhances the activity of standard of care therapies in erlotinib-sensitive and -resistant NSCLC models.](#)

Permanent Abstract Number: 2637

In *in vitro* studies with NSCLC and other cancer cell types, STA-9090 was found to significantly enhance the *in vitro* cytotoxicity of the taxanes, paclitaxel and docetaxel. Consistent with these results, STA-9090 dramatically enhanced the *in vivo* efficacy of paclitaxel in an erlotinib (Tarceva)-

resistant NSCLC model. In other models, STA-9090 also enhanced the *in vivo* efficacy of the EGFR inhibitor erlotinib and the anti-VEGF monoclonal antibody bevacizumab (Avastin). These combinations did not result in significant additional toxicity relative to the single agents alone, and pharmacokinetic analyses demonstrated that these findings were not due to drug-drug interactions.

STA-9090 significantly inhibits HIF-1a expression in the hypoxic regions of tumors

Poster Presentation April 19, 2:00 p.m. ET

Title: [Hsp90 inhibitor STA-9090 induces HIF-1a degradation in the hypoxic regions of solid tumors.](#)

Permanent Abstract Number: 2638

HIF-1a is the master regulator of the hypoxic tumor response and its expression has been correlated with resistance to radiation and chemotherapy and a propensity to metastasize. In contrast to many chemotherapies, STA-9090 efficiently penetrates deep into the hypoxic regions of solid tumors where it can potently down-regulate HIF-1a expression. In preclinical *in vivo* studies, a single dose of STA-9090 reduced HIF-1a expression by 6-fold at 24 hours after treatment.

STA-9090 potently inhibits JAK/STAT signaling

Poster Presentation April 19, 2:00 p.m. ET

Title: [Multimodal action of the Hsp90 inhibitor STA-9090 in treating cancer cells with activated JAK/STAT signaling.](#)

Permanent Abstract Number: 2640

The JAK kinases are established Hsp90 client proteins and there is evidence that JAK signaling occurs in a wide variety of cancer types. Mutations in JAK2 can result in the activation of the transcription factors STAT3 and STAT5, leading to cancer cell growth (oncogenesis). In *in vitro* and *in vivo* studies, STA-9090 potently inhibits the proliferation of numerous solid tumor and hematological cancer cell lines that are dependent upon persistent JAK/STAT signaling for growth and survival.

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 including IPI-504). 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 dasatinib (Sprycel^(R)).

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.

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, 2009 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.

SOURCE: Synta Pharmaceuticals Corp.

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