Synta Announces Publication of Results Showing Ganetespib (STA-9090) Exhibits Potent Activity in Models of Cancer with Activated JAK/STAT Signaling

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- Multiple cell signaling pathways simultaneously inhibited by ganetespib leads to superior activity than direct pan-JAK inhibitors -

- JAK/STAT signaling linked to cancer cell proliferation in wide range of cancers -

LEXINGTON, Mass., May 26, 2011 (BUSINESS WIRE) -- Synta Pharmaceuticals Corp. (NASDAQ: SNTA) today announced the publication in the on-line edition of the journal PLoS ONE (www.plosone.org/article/info:doi%2F10.1371%2Fjournal.pone.0018552) of results demonstrating that ganetespib, a potent second generation inhibitor of heat shock protein 90 (Hsp90), exhibits potent *in vitro* and *in vivo* activity in a range of solid and hematologic tumor cells that are dependent on Janus-associated kinase 2 (JAK2) activity for growth and survival.

"JAK2, a kinase associated with a broad range of cancers, is known to be dependent on Hsp90 for stability," said Vojo Vukovic, M.D., Ph.D., Senior Vice President and Chief Medical Officer, Synta Pharmaceuticals. "Our studies show that ganetespib potently inhibits JAK2, which in turn inhibits the Signal Transducers and Activators of Transcription (STAT) proteins that mediate a wide range of biological processes including cell growth, differentiation, apoptosis, inflammation and immune response. STAT3 and STAT5, in particular, are known to increase tumor cell proliferation, survival, metastasis and tumor-promoting inflammation in both solid and hematologic tumors. Ganetespib, by inducing the degradation of JAK2, inhibits these key drivers of cancer cell growth."

"Unlike direct JAK inhibitors, ganetespib also inhibits a number of other critical cancer-promoting factors such AKT, CDK1, CENP-E, WEE1 and numerous other genes involved in cell division and DNA replication," continued Dr. Vukovic. "The simultaneous inhibition of both the JAK/STAT pathway and related cancer-promoting pathways may be driving the superior activity seen in these models with ganetespib as compared to direct JAK inhibitors. These results provide additional evidence that ganetespib has the potential to be an important new therapeutic option for treating cancer either as a single agent or in combination with other anti-cancer agents."

Ganetespib is currently being studied in a broad range of clinical trials, with nearly 400 patients treated to date and a Phase 2b/3 trial in non-small cell lung cancer (NSCLC) expected to start in Q2 2011. Ganetespib is structurally unrelated to earlier Hsp90 inhibitors such as 17-AAG and has shown superior activity to these agents in preclinical studies. In clinical trials, ganetespib has shown single-agent activity in multiple tumor types and an absence of the serious liver and ocular toxicities seen with other Hsp90 inhibitors.

From *in vitro* studies, ganetespib was shown to inhibit JAK2-mediated signal transduction and proliferation in solid tumor cell lines as well as hematologic cancers driven by the $JAK2^{V617F}$ activating mutation, the most prevalent abnormality observed in *BCR-ABL1*-negative

myeloproliferative neoplasms. Results from transcript profiling studies showed that while both ganetespib and a JAK inhibitor were effective in modulating JAK/STAT target genes, only ganetespib altered the expression of a large set of genes involved in cell cycle-related activities, demonstrating an advantage over JAK-specific inhibitors. *In vivo*, ganetespib effectively increased survival in an orthotopic model of leukemia driven by $JAK2^{V617F}$ and induced significant tumor regression in STAT5-driven acute myeloid leukemia xenograft models due to the coordinated actions on STAT5 and cell cycle regulators.

About Ganetespib

Ganetespib (formerly STA-9090) is a potent, synthetic, small-molecule inhibitor of heat shock protein 90 (Hsp90). Hsp90 is a molecular chaperone required for the proper folding and activation of many cancer-promoting proteins, and is recognized as a key facilitator of cancer cell growth and survival. In preclinical experiments, ganetespib has shown activity in multiple tumor models both as a single agent and in combination with certain widely used cancer agents. Ganetespib is currently being evaluated in a broad range of cancer clinical trials. In these trials, ganetespib has shown clinical activity in heavily pretreated patients and has been well tolerated to date with no evidence of severe liver or common ocular toxicities seen with other Hsp90 inhibitors. The most common adverse event seen to date has been diarrhea, which has been manageable with standard supportive care. Information on clinical trials with ganetespib can be found at www.clinicaltrials.gov.

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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