



Synta Announces Publication of Clinical and Non-Clinical Results Demonstrating Unique Anti-angiogenic Effects of Ganetespib

July 17, 2013

– Results Suggest Targeting Hsp90 May Inhibit Angiogenesis without Tumor Rebound Effects Associated with VEGF-Targeted Anti-angiogenic Therapies –

– Support Rationale for Combining Ganetespib with Standard Anti-angiogenic Agents –

LEXINGTON, Mass.--(BUSINESS WIRE)--Jul. 17, 2013-- Synta Pharmaceuticals Corp. (NASDAQ: SNTA) announced today publication of results from in vitro, in vivo, and translational clinical studies demonstrating the effect of ganetespib on the ability of tumors to grow new blood vessels (angiogenesis). The paper appeared in the July 10, 2013, online issue of [Angiogenesis](#). Ganetespib, a selective inhibitor of the Hsp90 chaperone protein in development by Synta, is being evaluated in over 20 clinical trials for different types of cancer, including a pivotal Phase 3 trial in non-small cell lung cancer.

"To date two therapeutic strategies have been established for inhibiting new tumor blood vessel formation: agents that bind directly to vasculature growth factors (e.g., VEGF), or agents that bind to their cellular receptors (e.g., VEGFR)," said Dr. Bassel El-Rayes, Director of the GI Oncology Translational Research Program, Winship Cancer Institute, Emory University and senior author of the paper. "The results published this week show that ganetespib may offer a third way to suppress angiogenesis: inhibiting the transcription factors that turn on production of VEGF and other pro-angiogenic factors. This is like turning off the faucet at the source, rather than trying to empty the sink once it is full."

The publication describes results from preclinical studies and a rectal cancer clinical trial conducted at Emory University showing that ganetespib simultaneously downregulates the expression of many cellular proteins involved in new blood vessel formation, including VEGF, PDGFA, FGF2, Ang-1, Ang-2, TGFb1, HIF-1a, and STAT-3.

"Targeting angiogenesis with anti-VEGF therapies has demonstrated meaningful clinical benefit, but has also been associated with greater disease aggressiveness and metastasis from increased expression of VEGF-A and activation of HIF-1a in the hypoxic tumor," said Dr. El-Rayes. "These studies show that the unique mechanism of action of ganetespib may provide a means to downregulate angiogenesis without upregulating HIF-1a activation and VEGF expression. These effects strongly support the rationale to combine ganetespib with standard anti-angiogenic agents."

Previously presented results showed synergistic activity of ganetespib and the anti-angiogenic agent bevacizumab, an antibody targeting VEGF, in preclinical models of cancer.

About Ganetespib

Ganetespib, an investigational drug candidate, is a selective inhibitor of heat shock protein 90 (Hsp90), a molecular chaperone which controls the folding and activation of a number of client proteins that drive tumor development and progression. Many solid and hematologic tumors are dependent on Hsp90 client proteins including proteins involved in "oncogene addiction" (ALK, HER2, mutant BRAF and EGFR, androgen receptor, estrogen receptor, JAK2); proteins involved in resistance to chemotherapy and radiation therapy (ATR, BCL2, BRCA1/2, CDK1/4, CHK1, survivin, and WEE1); proteins involved in angiogenesis (HIF-1alpha, VEGFR, PDGFR, and VEGF); and proteins involved in metastasis (MET, RAF, AKT, MMPs, HIF-1alpha, and IGF-1R). In preclinical models, inhibition of Hsp90 by ganetespib results in the inactivation, destabilization, and eventual degradation of these cancer-promoting proteins. Ganetespib is being evaluated in over 20 clinical trials including trials in lung, breast, colorectal, and hematologic malignancies. Information on these trials 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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