Synta Announces Publications Demonstrating Ganetespib Activity in Triple-Negative Breast Cancer Models

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LEXINGTON, Mass.--(BUSINESS WIRE)--Nov. 21, 2013-- Synta Pharmaceuticals Corp. (NASDAQ: SNTA) announced two publications with results demonstrating the activity of ganetespib in preclinical models and in a clinical treatment setting of triple-negative breast cancer (TNBC). Ganetespib is a potent and selective inhibitor of the Hsp90 chaperone protein being evaluated in over 25 clinical trials, including a pivotal Phase 3 trial in non-small cell lung cancer.

The results demonstrate the ability of ganetespib to down-regulate a number of key proteins involved in tumor growth and metastasis. Results by Synta collaborators at Johns Hopkins University were published on-line in the *Journal of Molecular Medicine* and results by Synta scientists and collaborators at Dana-Farber Cancer Institute and Duke University were published in *Clinical Cancer Research*:

- “Ganetespib blocks HIF-1 activity and inhibits tumor growth, vascularization, stem cell maintenance, invasion, and metastasis in orthotopic mouse models of triple-negative breast cancer” by Lisha Xiang, Daniele M. Gilkes, Pallavi Chaturvedi, Weibo Luo, Hongxia Hu, Naoharu Takano, Houjie Liang, and Gregg L. Semenza, *Journal of Molecular Medicine*
- “Preclinical activity profile and therapeutic efficacy of the Hsp90 inhibitor ganetespib in triple-negative breast cancer” by David A. Proia, Chaohua Zhang, Manuel Sequeira, John-Paul Jimenez, Suqin He, Neil L. Spector, Geoffrey I. Shapiro, Sara Tolaney, Masazumi Nagai, Jaime Acquaviva, Donald L. Smith, Jim Sang, Richard C. Bates, and Iman El-Hariry, *Clinical Cancer Research*

A particularly sensitive protein to ganetespib treatment is HIF-1alpha, a major regulator of multiple tumor growth properties, including angiogenesis (tumor blood vessel development), metastasis (cancer spread), metabolism, cancer stem cell maintenance, and invasion. The results demonstrate that inhibition of a wide collection of protein targets, including HIF-1alpha, correlate with potent effects on TNBC tumor cell viability and metastasis when ganetespib is administered as monotherapy or when combined with routinely used chemotherapeutics for treatment of TNBC, including doxorubicin, paclitaxel, and docetaxel.

As previously reported by Synta, clinical activity was also observed along with a favorable toxicity profile in two TNBC patients treated with ganetespib monotherapy in the company-sponsored ENCHANT-1 Phase 2 trial.

References for both publications are available on the Synta Pharmaceuticals website.

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, and 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, PDFGR, 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 trials in lung cancer, breast cancer, and other tumor types. The most common adverse event seen to date has been transient, mild or moderate diarrhea, which has been manageable with standard supportive care. Information on these trials can be found at www.clinicaltrials.gov. Ganetespib has received Fast Track designation from FDA for second-line treatment of non-small cell lung adenocarcinoma in combination with docetaxel.

About the ENCHANT-1 Clinical Trial

ENCHANT-1 is a proof-of-concept, ”window-of-opportunity” trial designed to evaluate single-agent ganetespib safety and clinical activity in locally advanced or first line metastatic HER2-positive and triple-negative breast cancer. The trial will also evaluate the combination of ganetespib with paclitaxel. More information about this trial can be found at www.clinicaltrials.gov (NCT01677455)

About Breast Cancer

Breast cancer is the most frequent cancer in women, accounting for 458,000 deaths worldwide in 2008, according to the World Health Organization. In the U.S., the American Cancer Society estimates that about 297,000 cases of breast cancer will be diagnosed in 2013. Breast cancer is often characterized in the context of three biomarkers: ER/PR positive, HER2-positive, or negative for all three (triple-negative). Standard treatment for the first two categories includes therapies targeting hormonal or HER2 signaling pathways. There are no established targeted therapies for patients with triple-negative disease, which accounts for approximately 15% of all breast cancer and is associated with poor patient prognosis.

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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