Ganetespib Shows Clinical Activity in HER2+ and Triple Negative Metastatic Breast Cancer

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-Phase 2 Trial Results Presented at San Antonio Breast Cancer Symposium-
-15% response rate as single-agent in HER2+ patients who had progressed on trastuzumab-
-Development to continue in HER2+ and triple-negative patients in new combination trial-

LEXINGTON, Mass., Dec 08, 2011 (BUSINESS WIRE) -- Synta Pharmaceuticals Corp. (NASDAQ: SNTA) - Ganetespib, a potent, second generation Hsp90 inhibitor, has demonstrated clinical activity in heavily pre-treated patients with HER2-positive and triple negative metastatic breast cancer according to Phase 2 clinical trial results presented by researchers from Memorial Sloan-Kettering Cancer Center at the San Antonio Breast Cancer Symposium (SABCS).

"The single agent ganetespib results presented today further validates Hsp90 as a target for treating HER2-positive breast cancer and suggest Hsp90 inhibition may be an important new approach to treating triple negative breast cancer," said Shanu Modi, M.D., Memorial Sloan-Kettering Cancer Center, the principal investigator on this study. "15% (2/13) of the patients with the HER2 gene amplification experienced a partial response in this trial and an additional 46% (6/13) achieved stable disease. These encouraging results for Hsp90 inhibition in HER2 positive disease are consistent with results from an earlier Phase 2 study of 17-AAG, a first generation Hsp90 inhibitor, in which 22% (6/27) achieved partial response and an additional 37% (10/27) achieved stable disease[1]. While in the prior study 17-AAG was given in combination with trastuzumab, in the current study ganetespib was given as a monotherapy. Together, these studies present compelling evidence that Hsp90 inhibition is effective in HER2-positive breast cancer."

"We were also encouraged by evidence of clinical activity in one of three evaluable triple negative breast cancer patients, who experienced significant tumor shrinkage following three doses of ganetespib," continued Dr. Modi. "Triple-negative breast cancer represents a difficult-to-treat disease, for which no targeted therapies are currently approved."

All HER2-positive patients on the ganetespib Phase 2 trial had progressed following treatment with trastuzumab (Herceptin®).

"We are excited to continue development with this compound in a Phase 1/2 combination trial," continued Dr. Modi. "This new trial will evaluate ganetespib in combination with paclitaxel and trastuzumab in HER2-positive breast cancer, and ganetespib in combination with paclitaxel in triple negative breast cancer. "Ganetespib has demonstrated synergy with taxanes in pre-clinical studies and is currently being studied in a Phase 2b/3 trial in combination with docetaxel in non-small cell lung cancer. The Phase 1/2 trial in breast cancer will be initiated in 2012.

"The evidence of single agent activity shown today is supported by earlier ganetespib clinical results, including a confirmed, objective response in the triple-negative breast cancer patient

enrolled in our Phase 1 trial," said Iman El-Hariry, M.D., Ph.D., Vice President, Clinical Research, Synta. "Importantly, ganetespib was well-tolerated in this trial Phase 2 trial with Grade 1 and 2 diarrhea and fatigue being the most commonly reported adverse events. This is consistent with the safety profile seen in over 450 patients treated to date across a wide range of cancers. The activity reported today combined with a favorable safety profile supports advancing both the MSKCC combination trial as well as additional proof-of-concept trials of ganetespib in HER2-positive and triple negative breast cancer."

A total of 22 patients were enrolled in the trial reported today. Of the 13 HER2+ patients, all of whom were refractory to treatment with trastuzumab, 2/13 (15%) showed a partial response, and an additional 6/13 (46%) showed stable disease as their best response.

About HER2-positive Breast Cancer

HER2-positive breast cancer is a subtype of breast cancer that tests positive for over-expression of a protein called human epidermal growth factor receptor 2 (HER2), which promotes the growth and progression of cancer cells. In about 1 of every 5 breast cancers, the cancer cells make an excess ("over-expression") of HER2 due to a gene mutation.

About Triple-negative Breast Cancer

Triple-negative breast cancer is a subtype of breast cancer that tests negative for expression of estrogen and progesterone receptors (ER/PR) and HER2 protein. It is characterized by its aggressive behavior, distinct patterns of metastasis, and lack of approved targeted therapies.

1. Shanu Modi, Alison Stopeck, Hannah Linden, David Solit, Sarat Chandarlapaty, Neal Rosen, Gabriella D'Andrea, Maura Dickler, Mary E. Moynahan, Steven Sugarman, Weining Ma, Sujata Patil, Larry Norton, Alison L. Hannah, Clifford Hudis: **HSP90 Inhibition is Effective in Breast Cancer: A Phase 2 Trial of Tanespimycin (17AAG) plus Trastuzumab in Patients with HER2-Positive Metastatic Breast Cancer Progressing on Trastuzumab**. Clin Cancer Res, May 10, 2011.
2. Baselga J, Tripathy D, Mendelsohn J, Baughman S, Benz CC, Dantis L, Sklarin NT, Seidman AD, Hudis CA, Moore J, Rosen PP, Twaddell T, Henderson IC, Norton L: **Phase II study of weekly intravenous recombinant humanized anti-p185HER2 monoclonal antibody in patients with HER2/neu-overexpressing metastatic breast cancer**. J Clin Oncol 1996, 14:737-744.
3. Cobleigh MA, Vogel CL, Tripathy D, Robert NJ, Scholl S, Fehrenbacher L, Wolter JM, Paton V, Shak S, Lieberman G, Slamon DJ: **Multinational study of the efficacy and safety of humanized anti-HER2 monoclonal antibody in women who have HER2-overexpressing metastatic breast cancer that has progressed after chemotherapy for metastatic disease**. J Clin Oncol 1999, 17:2639-2648.

About Hsp90

Hsp90 is a chaperone protein required for the proper folding and activation of cellular proteins, particularly kinases. Many of these "client proteins" of Hsp90 - such as ALK, 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.

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, including the global Phase 2b/3 GALAXY trial in non-small cell lung cancer. In these trials, ganetespib has shown anti-tumor activity in heavily pretreated patients with lung cancer, breast cancer, and other tumor types and has been well tolerated 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 http://clinicaltrials.gov/ct2/results?term=ganetespib.

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 http://www.syntapharma.com.

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