



## Synta Announces ENCHANT-1 Breast Cancer Results Support Transition to Second Stage of Trial

July 29, 2013

*– Trial evaluating ganetespib monotherapy in HER2-positive and triple-negative breast cancer meets preplanned expansion criteria –*

*– Complete clinical response and surgical restaging in TNBC patient following treatment with single-agent ganetespib --*

LEXINGTON, Mass.--(BUSINESS WIRE)--Jul. 29, 2013-- Synta Pharmaceuticals Corp. (NASDAQ: SNTA) announced today that preliminary results from the ENCHANT-1 clinical trial, which evaluates ganetespib monotherapy in patients with newly diagnosed locally advanced or metastatic HER2 positive or triple-negative breast cancer (TNBC), achieved the prespecified criteria for advancing to the second stage of the trial.

Of the initial five HER2-positive patients enrolled in the study, two achieved objective tumor response and two achieved stable disease (SD) within the three cycles of treatment on study (12 weeks). Of the initial ten TNBC patients enrolled and evaluable for response, two achieved objective tumor response and three achieved SD following treatment with ganetespib monotherapy.

ENCHANT-1 is a 'window-of-opportunity' study designed to evaluate the clinical activity of single-agent ganetespib over a 12-week period preceding standard first line treatment. The protocol specifies advancing to the second stage of enrollment in each cohort if there was at least one objective tumor response out of the initial fifteen evaluable patients specified for Stage 1. This criterion was achieved in both cohorts, and therefore both cohorts will continue to enroll patients up to a total of 33 evaluable patients per cohort.

Metabolic response was also assessed in the study, by comparing baseline and week 3 PET scans. Of the five HER2-positive patients, four achieved metabolic responses. Of the 13 TNBC patients with post-baseline PET scans, six achieved metabolic response.

"Ganetespib appears to be what many of us in the Hsp90 field have been seeking for many years: a well tolerated, highly potent Hsp90 inhibitor that is clinically active in tough-to-treat cancers," said Dr. Neil Spector, Co-Director of Developmental Therapeutics Program, Duke University and an investigator on the trial. "Given the known role of Hsp90 in fueling breast cancer growth and metastasis, and the single-agent activity seen with ganetespib, I believe this compound has potential to be an important new therapy for women with breast cancer."

Among the patients enrolled in the study is a 68 year old woman diagnosed with inoperable TNBC, including extensive disease that had spread to her lymph nodes. The week 3 PET scan showed metabolic response in all lesions and the week 12 physical exam showed no evidence of tumor. Treatment was adjudicated a complete clinical response, and her disease was restaged from

inoperable to operable. Earlier this month, she successfully completed a mastectomy with curative intent.

“It is quite remarkable to see such a strong clinical response in this devastating disease, particularly with a single-agent regimen this well tolerated,” said Dr. Tamas Hickish, Professor at the Royal Bournemouth Hospital, Dorset, UK, the treating physician and an investigator on the study. “This outcome strongly supports the further investigation of ganetespib either as a single-agent or in combination with standard of care treatments used in this setting.”

Consistent with prior experience in over 700 patients treated with ganetespib to date, the most common adverse event seen with ganetespib in the ENCHANT-1 trial was mild to moderate, transient diarrhea, which was generally manageable with standard medication.

“These encouraging findings confirm prior signals of clinical activity seen with ganetespib in breast cancer,” said Dr. Iman El-Hariry, Vice President of Clinical Research at Synta. “The favorable safety profile, clear single-agent clinical activity, and strong rationale for combination therapy suggest ganetespib may have broad potential utility in breast cancer. Taxanes in particular are widely used in breast cancer. The positive results for the combination of ganetespib with docetaxel in lung cancer provide strong rationale for exploring the taxane combination regimen in breast cancer as well.”

The expansion of the ENCHANT-1 trial will also allow for evaluation of the combination of weekly paclitaxel and ganetespib. Separately, an investigator-sponsored study evaluating the combination of ganetespib, paclitaxel, and trastuzumab in HER2-positive patients is initiating at MSKCC and NYU.

Results from ENCHANT-1 are expected to be presented at a medical meeting later this year.

### **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 a Phase 3 trial in non-small cell lung adenocarcinoma, as well as additional trials in lung, breast, colorectal, and hematologic malignancies. Information on these trials can be found at [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

### **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](http://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](http://www.syntapharma.com).

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Source: Synta Pharmaceuticals Corp.

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