



## **Synta Announces Launch of GANNET53, a Randomized, pan-European Study of Ganetespib in p53 Mutant, Metastatic Ovarian Cancer**

January 9, 2014

*Study sponsored by Innsbruck Medical University in Austria and funded by the European Commission*

LEXINGTON, Mass.--(BUSINESS WIRE)--Jan. 9, 2014-- Synta Pharmaceuticals Corp. (NASDAQ: SNTA) today announced the launch of GANNET53, a pan-European randomized trial evaluating the combination of ganetespib and paclitaxel vs. paclitaxel alone in over 200 patients with metastatic, predominantly p53 mutant, platinum-resistant ovarian cancer. Centers in Austria, Belgium, France, and Germany will participate in the clinical trial, which is expected to begin enrollment in mid-2014. Ganetespib, Synta's lead anti-cancer drug candidate, inhibits the heat shock protein 90 (Hsp90) chaperone protein and is being studied in over 25 clinical trials, including an ongoing Phase 3 trial in advanced non-small cell lung cancer.

Approximately 70% of advanced ovarian cancers are characterized as Type II tumors, which exhibit mutations in the p53 tumor suppressor gene and are associated with particularly aggressive, rapid disease progression. Preclinical models have shown that mutant p53 is critical to the growth and proliferation of these cancers. Many mutations render p53 unable to fold appropriately, leaving the protein highly dependent on Hsp90 for stability. Inhibition of Hsp90 destroys the complex between Hsp90 and mutant p53, leading to the degradation of the protein and cancer cell death. This anti-cancer activity is substantially stronger in cells with mutant p53 than in cells with non-mutated p53, suggesting potential as a predictive biomarker for Hsp90 inhibitors such as ganetespib.

Hsp90 inhibition has also been shown to sensitize mutant p53 cancer cells to treatment with chemotherapies, as has been seen in preclinical studies evaluating ganetespib in other tumor types, supporting the planned trial design evaluating the combination of ganetespib and paclitaxel vs. paclitaxel alone.

"There is a pressing need for more effective, innovative treatment strategies to improve survival in this group of epithelial ovarian cancer patients," said Professor Nicole Concin of the Innsbruck Medical University in Austria and the GANNET53 trial Principal Investigator. "The GANNET53 trial aims to achieve this goal by using ganetespib to target mutant p53, which may be a central driver of ovarian cancer aggressiveness and metastatic ability. This approach is supported by the preclinical findings as well as encouraging clinical results for ganetespib, including durable objective tumor responses observed with ganetespib monotherapy in cancers with genetic profiles driven by strong Hsp90 clients, as well as the favorable activity and safety profile observed for the combination of ganetespib and taxanes."

"The selection of ganetespib for the GANNET53 program and the European Commission support are exciting steps in advancing both the science and clinical potential of ganetespib," said Safi R. Bahcall, Ph.D., President and CEO of Synta. "The identification and evaluation of the connection between p53 mutation status and the potential role for Hsp90 inhibition, may have important implications not only for patients with ovarian cancer, but in other tumor types for which p53 mutation is known to be important, such as triple-negative breast cancer."

Additional information on the ovarian cancer scientific findings and the GANNET53 program are available at [www.gannet53.eu](http://www.gannet53.eu) and at [www.clinicaltrials.gov](http://www.clinicaltrials.gov). Additional information on the combination of ganetespib and taxanes is available at [www.syntapharma.com](http://www.syntapharma.com).

Synta has established over 100 academic, preclinical collaborations investigating the science and potential applications of ganetespib. Over two dozen clinical trials sponsored by investigators, cooperative groups, or patient foundations are ongoing or planned for 2014.

### **About Ovarian Cancer**

Each year, approximately 230,000 new cases of ovarian cancer are diagnosed worldwide. Ovarian cancer is the most deadly of the gynecologic cancers, causing approximately 140,000 deaths worldwide each year, including 41,900 deaths in Europe and 14,000 deaths in the US. The serous ovarian cancer subtype, a particularly aggressive form driven by mutations of p53 (an Hsp90 client protein), makes up 75 to 80% of diagnoses, with approximately 70% of these cases diagnosed in stage III or IV. Platinum-based chemotherapy remains the mainstay of therapy and results in a 5-year survival rate of only 30% and 10% for stages III and IV, respectively.

### **About GANNET53**

GANNET53 (Ganetespib in metastatic, p53 mutant, platinum-resistant ovarian cancer) is a Seventh Framework Programme for Research (FP7) project sponsored by the Innsbruck Medical University and funded by the European Commission. This pan-European, multi-center trial is designed to determine the efficacy of ganetespib and paclitaxel compared to paclitaxel alone in patients with metastatic, Type II, platinum-resistant ovarian cancer, which is characterized by mutations in the p53 gene. The GANNET53 trial is the result of a preclinical research collaboration between members of the European consortium conducting the study and Synta. For additional information, please visit [www.gannet53.eu](http://www.gannet53.eu).

### **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, 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 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](http://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 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)

#### **Safe Harbor Statement**

This media release may contain forward-looking statements about Synta Pharmaceuticals Corp. Such forward-looking statements can be identified by the use of forward-looking terminology such as "will", "would", "should", "expects", "anticipates", "intends", "plans", "believes", "may", "estimates", "predicts", "projects", or similar expressions intended to identify forward-looking statements. Such statements, including statements relating to enrollment of the GANNET53 trial, reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such forward-looking statements, including those described in "Risk Factors" of our Form 10-K for the year ended December 31, 2012 as filed with the Securities and Exchange Commission. Synta undertakes no obligation to publicly update forward-looking statements, whether because of new information, future events or otherwise, except as required by law.

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