Synta Announces Ganetespib Presentations at the Annual Meeting of the American Society for Clinical Oncology

June 4, 2012

–Potent activity in preclinical models of ALK, ROS1, and RET+ lung cancer–

–Superior activity to direct ALK inhibitors in both crizotinib-sensitive and -resistant models–

–Reduced rate of ocular toxicity observed in clinical trials compared to other Hsp90 inhibitors correlates with physiochemical properties–

LEXINGTON, Mass.--(BUSINESS WIRE)--Jun. 4, 2012-- Synta Pharmaceuticals Corp. (NASDAQ: SNTA) today announced results from studies evaluating the Company's lead drug candidate, ganetespib, a potent second-generation Hsp90 inhibitor, presented at the annual meeting of the American Society for Clinical Oncology (ASCO).

"We believe results presented at the ASCO conference this year further validate the high clinical potential of ganetespib for the treatment of oncologic indications," said Vojo Vukovic, Chief Medical Officer of Synta. "In contrast with ganetespib or 17-AAG, a number of other Hsp90 inhibitors have shown a high incidence of ocular toxicity in patients. Results presented today from preclinical experiments show that physicochemical properties associated with penetration and accumulation in retina correlate with observed clinical ocular toxicity seen with other Hsp90 inhibitors."

"In addition to results supporting the observed favorable clinical safety profile for ganetespib, other findings presented today establish exciting potential for Hsp90 inhibition in ALK+, ROS1+, and RET+ lung cancer," continued Dr. Vukovic. "These results support our parallel development approach for ganetespib entailing both monotherapy and combination treatment evaluation across multiple cancer indications. Results from our Phase 1 combination study of ganetespib and docetaxel, updated today, were used to inform the choice of dose and schedule in our ongoing Phase 2b/3 GALAXY study in second-line non-small cell lung cancer."

All ganetespib posters are available at www.syntapharma.com.

Ganetespib activity in ALK+ and other forms of non-small cell lung cancer

Title: Preclinical activity of the Hsp90 inhibitor, ganetespib, in ALK- and ROS1-driven cancers.
Presenter: David Proia, Ph.D., Synta Pharmaceuticals
Poster Presentation: Monday, June 4, 8:00 am -12:00 pm CT - Hall A2
ASCO abstract #3090

In a commonly used ALK+ NSCLC cell line, ganetespib was shown to cause the loss of expression of the EML4-ALK fusion protein, the primary driver of this disease, as well as expression of a number of other Hsp90 client proteins implicated in tumor growth. This effect was consistent with the

profoundly greater impact that ganetespib had on delaying tumor growth in ALK+ xenograft models compared with crizotinib, a direct ALK inhibitor, or vehicle alone. When combined, ganetespib and crizotinib exhibited a synergistic cell killing effect greater than when either drug was used alone. Furthermore, ganetespib remained just as active against a “wild-type” ALK+ cell line as it did upon a wide collection of derived cell lines harboring different secondary ALK mutations that render resistance to crizotinib. Finally, a transition state known to be associated with the genesis of tumor metastases (EMT) was observed with prolonged crizotinib treatment, but not with ganetespib treatment. Separately, ganetespib also demonstrated potent activity against growth of cell lines driven by aberrant ROS1 and RET oncogene activity. These results support utility in a range of oncogene-addicted NSCLC tumor settings either as a monotherapy or in combination.

Synta recently initiated the Phase 2 CHIARA trial – Evaluating **CH**aperone **I**nhibition in **A**lk **R**earranged lung c**A**ncer – to evaluate ganetespib monotherapy in 110 advanced ALK+ NSCLC patients not previously treated with ALK inhibitor therapy. A trial evaluating the combination of crizotinib and ganetespib in patients with ALK+ NSCLC not previously treated with ALK inhibitor therapy was recently initiated at Memorial Sloan Kettering Cancer Center in New York. Other trials evaluating ganetespib in ALK+ NSCLC are under discussion.

“The development of compounds targeting ALK kinase directly has been a major advance for patients with ALK+ disease,” said Dr. Vukovic. “However, many ALK+ patients respond inadequately to monotherapy treatment with ALK kinase inhibitors, leaving significant room for improvement. Hsp90 inhibition offers an entirely new and complementary treatment option for these patients, which could ultimately lead to enhanced duration of clinical benefit.”

Retinal / Plasma drug exposure ratio and elimination are associated with ocular toxicity profiles of select Hsp90 inhibitors

Title: Associating Retinal Drug Exposure and Retention with the Ocular Toxicity Profiles of Hsp90 Inhibitors.
Presenter: Dan Zhou, M.D., M.M., Synta Pharmaceuticals
Poster Presentation: Monday, June 4, 8:00 am -12:00 pm CT - Hall A2
ASCO abstract #3086

Ocular toxicities in up to 89% of patients, including blurred vision, flashes, delayed light/dark accommodation, and photophobia have been reported in human clinical trials with certain Hsp90 inhibitors, including 17-DMAG, AUY922 and SNX-5422. These adverse events are believed to be due to drug-induced retinal photoreceptor degeneration and cell death based on previously reported studies in preclinical animal models. In contrast, little to no ocular toxicity has been observed in clinical trials evaluating the Hsp90 inhibitors ganetespib and 17-AAG.

To understand these differences in further detail, this study examined the relationship between retinal drug distribution profiles and degree of photoreceptor cell death following administration of these Hsp90 inhibitors. Profiles of 17-DMAG and AUY922 were compared with those of ganetespib and17-AAG (and vehicle control) in rats. 17-DMAG and AUY922 produced marked photoreceptor cell death, consistent with previous observations, and were associated with a slow elimination rate and a high retina/plasma (R/P) ratio. In contrast, ganetespib and 17-AAG did not accumulate appreciably in animal retinas nor produce detectable photoreceptor injury, consistent with the near absence of visual abnormalities patients treated with these two agents.

Ganetespib/docetaxel combination in solid tumors

Title: A Phase 1 and Pharmacokinetic Study of Ganetespib (STA-9090), a Heat Shock Protein 90 Inhibitor, in Combination with Docetaxel in Subjects with Advanced Solid Tumor Malignancies.
Presenter: John Kauh, M.D., Emory University School of Medicine
Poster Presentation: Monday, June 4, 8:00 am -12:00 pm CT - Hall A2
ASCO abstract #3094

Updated results were presented from a dose-escalation Phase 1 study evaluating the combination of ganetespib plus docetaxel in patients with advanced solid tumors. Primary study objectives included determining recommended dose, schedule, safety and tolerability of the docetaxel/ganetespib combination for clinical evaluation going forward.

Twenty-seven patients were enrolled in schedules A (n=12) docetaxel 60 mg/m^2, ganetespib 150 mg/m^2, B (n=8) docetaxel 75 mg/m^2, ganetespib 150 mg/m^2, and C (n=7) docetaxel 75 mg/m^2, ganetespib 200 mg/m^2. Tumor types included NSCLC (n=9), head & neck (n=4), and small cell lung (n=3) cancers. The maximum tolerated dose was defined as docetaxel 75 mg/m^2 and ganetespib 150 mg/m^2. The median number of cycles received was 2 (1-11). Among 22 patients evaluable for response, one patient with head & neck cancer had a partial response.

Common AEs included neutropenia, diarrhea, anemia, fatigue, nausea, and febrile neutropenia, consistent with what has been observed before with docetaxel and ganetespib administration. The recommended doses of docetaxel 75 mg/m^2 on day 1 and ganetespib 150 mg/m^2 on days 1 and 15 of a 21-day cycle were well tolerated. This schedule is being evaluated in the ongoing GALAXY study enrolling NSCLC patients who have failed one prior treatment regimen.

About Ganetespib

Ganetespib is a potent inhibitor of heat shock protein 90 (Hsp90) that is structurally unrelated to first-generation, ansamycin-related Hsp90 inhibitors. 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. In these trials, ganetespib has shown clinical activity in heavily pretreated patients and has been well tolerated with no evidence of severe liver or common ocular toxicities seen with other Hsp90 inhibitors to date. The most common adverse event seen with ganetespib has been transient, mild or moderate diarrhea, which has been manageable with standard supportive care. Ganetespib is being evaluated in over 20 clinical trials either ongoing or currently initiating. Information on these and other clinical trials can be found at www.clinicaltrials.gov.

About the GALAXY Trial™

The GALAXY (**G**anetespib **A**ssessment in **L**ung c**A**ncer with doceta**X**el) trial is a randomized Phase 2b/3 trial comparing the combination of ganetespib and docetaxel versus docetaxel alone in patients with Stage IIIB/IV NSCLC who have received one prior systemic therapy. Improvement in progression-free survival is the primary endpoint of the first stage, Phase 2b portion of the study. Results from this stage of the study will be used to inform design of the second stage, Phase 3 portion. More information about the GALAXY trial can be found at www.clinicaltrials.gov.

About the CHIARA Trial

The CHIARA (**CH**aperone **I**nhibition in **A**lk **R**earranged lung c**A**ncer) trial is a single arm, Phase 2 study evaluating ganetespib monotherapy in patients with Stage IIIB/IV non-small-cell lung cancer harboring an ALK gene rearrangement and who have not been previously treated with a direct ALK inhibitor. The primary endpoint of the study is objective response rate. A total of 110 patients are planned for accrual. More information about the CHIARA trial can be found at www.clinicaltrials.gov.

About 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. Many of the “client proteins” of Hsp90 – such as ALK, AKT, BCR-ABL, BRAF, KIT, MET, EGFR, FLT3, HER2, PDGFRA, VEGFR 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 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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Source: Synta Pharmaceuticals Corp.

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