Synta Announces Positive Overall Survival Results From GALAXY-1 Phase 2b/3 Trial of Ganetespib in Second-Line Non-Small Cell Lung Cancer

June 3, 2013

– Data presented at ASCO 2013 –

– Median overall survival improved 32% in the all adenocarcinoma, intent-to-treat population –

– In the population selected for the ongoing GALAXY-2 Phase 3 trial, median overall survival improved 67%, Hazard Ratio = 0.61 (p=0.009) –

– Webcast scheduled for 7:00 PM CDT –

CHICAGO--(BUSINESS WIRE)--Jun. 3, 2013-- Synta Pharmaceuticals Corp. (NASDAQ: SNTA) today announced results from an interim survival analysis of the GALAXY-1 trial, a global, randomized, multi-center Phase 2b/3 study designed to evaluate the efficacy and safety of the Company's lead drug candidate, the Hsp90 inhibitor ganetespib, as second-line treatment for patients with advanced non-small cell lung adenocarcinoma. The results show that the combination of ganetespib (G) plus docetaxel (D) improves overall survival (OS) and progression-free-survival (PFS) compared to docetaxel alone. The results also show that these improvements are enhanced in the pre-specified patient population that was selected last year for evaluation in the ongoing GALAXY-2 Phase 3 trial.

The results will be presented today at 5:15 PM CDT during an oral session at the 2013 meeting of the American Society of Clinical Oncology (ASCO) in Chicago by Dr. Suresh Ramalingam, M.D., Professor, Hematology & Medical Oncology, and Director, Division of Medical Oncology, of the Winship Cancer Institute of Emory University. Slides accompanying a morning ASCO press briefing will be available at 8:15 AM CDT on the company website at www.syntapharma.com.

"The goal of the GALAXY-1 trial was to select the patient population that would derive robust benefits with the novel combination," said Dr. Ramalingam. "The activity in patients with diagnosis of advanced disease greater than 6 months, together with the encouraging safety profile, suggest that ganetespib plus docetaxel has potential to be the first combination therapy for second-line treatment of adenocarcinoma of the lung."

"The two-stage, adaptive design of the GALAXY program balances the need to move quickly in developing a potential new therapy for severely ill patients, with the equally important objective of derisking Phase 3," said Safi R. Bahcall, PhD, President and CEO, Synta. "The results presented today reinforce this approach, confirming the selection of patient population for our ongoing GALAXY-2 Phase 3 trial, and increasing the likelihood of achieving our goal of bringing ganetespib to patients as rapidly as possible."

Results from interim analysis

The GALAXY-1 trial consists of two enrollment stages: a primary enrollment stage, which completed in November 2012 with 252 adenocarcinoma patients, and an extension enrollment stage for those patients with certain biomarker disease characteristics, which completed enrollment in May 2013 with an additional 70 patients. Interim analyses of overall survival from the primary adenocarcinoma enrollment stage were specified six and twelve months from the last patient enrolled. Data lock for the six-month follow-up analysis was May 15, 2013. As specified in the clinical trial protocol, analysis of the biomarker-defined patient populations will occur upon maturity of data from both the primary and extension enrollment stages, expected later this year.

Presented below are OS and PFS, in both the 252-patient all adenocarcinoma population (intent-to-treat; ITT) and the pre-specified patient population that was selected last year for evaluation in the ongoing GALAXY-2 Phase 3 trial: time since diagnosis of advanced disease greater than 6 months (“diagnosis > 6 months”). Patient baseline demographics, as well as post-study therapy, were generally well balanced between the two arms of the study for both populations.

Safety and efficacy results were reviewed by an independent data review committee consisting of a biostatician and four medical oncologists who did not participate in GALAXY-1.

	All Adenocarcinoma, ITT Population (N=252)		**Diagnosis of Advanced Disease > 6 Months Population* (N=176)**	
	D N=127	G+D N=125	D N=89	G+D N=87
Overall survival				
# events (%)	70 (55)	64 (51)	51 (57)	41 (47)
Median (months)	7.4	9.8	6.4	10.7
Unadjusted HR (90% CI)**	0.82 (0.62, 1.09), p=0.082		0.61 (0.43, 0.87), p=0.0093	
Cox-regression HR (90% CI)***	0.73 (0.55, 0.98), p=0.041		0.55 (0.38, 0.79), p=0.0036	
Progression-free survival				
# events (%)	90 (71)	90 (72)	63 (71)	59 (68)
Median (months)	3.2	4.5	3.4	5.4
Unadjusted HR (90% CI) **	0.84 (0.65, 1.07), p=0.038		0.61 (0.45, 0.83), p=0.0041	
Cox-regression HR (90% CI)***	0.83 (0.64, 1.06), p=0.108		0.62 (0.45, 0.86), p=0.0075	

* Population selected for evaluation in the ongoing GALAXY-2 Phase 3 trial. Diagnosis > 6 months generally excludes patients who experienced rapid worsening of disease during first-line therapy.

** Hazard ratio (HR) is an estimate of comparative risk between the two treatment groups. A hazard ratio of 1 can be interpreted as no decrease in risk, while an OS hazard ratio of 0.61 can be thought of as a 39% reduction in risk of dying as compared to the control group. P-values are calculated using the 1-sided stratified log-rank test.
*** Variables used in the pre-specified Cox regression analysis to assess and adjust for any potential imbalances in prognostic factors were: gender, smoking status, LDH, ECOG performance status, interval since diagnosis advanced disease, age, total baseline target lesion size, and geographic region (Eastern Europe vs. other).

Five pre-specified subpopulations were defined by enrollment stratifications and biomarker endpoints in GALAXY-1: mutant KRAS, elevated LDH, ECOG performance status, smoking status, and time since diagnosis of advanced disease (< 6 months vs. > 6 months). Consistent with results presented last year, time since diagnosis of advanced disease showed meaningful predictive value for overall survival improvement with ganetespib (test for interaction with study treatment: p=0.0064).

Tumor genetic markers were also evaluated in this analysis. 202 patients had sufficient tissue available for testing for KRAS mutation; of those 63 (31%) tested positive. 154 patients had sufficient remaining tissue for testing for an additional 65-gene panel of exploratory biomarkers; of those, 20 (13%) tested positive for EGFR mutation. The observed overall survival improvement between the combination arm and control arm did not correlate with either KRAS or EGFR mutational status. Analysis of additional exploratory biomarkers is ongoing.

Overall response rate (ORR) was also improved in the G+D arm compared to the D arm, in both the all-adenocarcinoma population and the diagnosis greater than 6 months populations. In the all-adenocarcinoma population, confirmed ORR improved from 9% to 14% (p=0.15). In the diagnosis greater than 6 months population, confirmed ORR improved from 9% to 15% (p=0.16).

“The results presented today are exciting in indicating the potential for creating a new treatment option for patients with progressive disease and limited treatment options,” said Dr. Philip Bonomi, Rush University Medical Center. “In addition, the results today provide convincing evidence for using rate of disease progression as a criterion for treatment selection. Similar criteria are increasingly common in other cancer types including breast, ovarian, and hematologic malignancies.”

“Outside of certain genetically-defined patient populations, there have been no new options for the treatment of patients with non-small cell adenocarcinoma following first-line therapy in nearly a decade,” said Dr. Dean A. Fennell, University Hospital, Leicester, UK, co-Principal Investigator of GALAXY-1. “The magnitude and consistency of the activity reported today are very encouraging and bode well for the outcome of the GALAXY-2 Phase 3 study.”

Ganetespib and new lesion growth

A separate ASCO meeting abstract (e19097) reported preclinical results related to the ability of ganetespib to reduce cancer cell invasiveness and metastatic potential. These results are consistent with preclinical results from other groups on the role of Hsp90 in tumor invasiveness, angiogenesis, and metastasis [1-4].

In the GALAXY-1 trial, time to appearance of new lesions (TTNL) measured time from randomization until a new metastatic lesion was reported. In the diagnosis > 6 months population, TTNL increased

from 6.9 months (D) to 11.3 months (G+D), with hazard ratio 0.5 (p=0.0053). This exploratory analysis suggests ganetespib may reduce the risk of emergence of new metastatic lesions by 50%. TTNL has been specified as a secondary endpoint in the ongoing GALAXY-2 Phase 3 trial.

Safety

The safety profile of patients treated with the combination of ganetespib and docetaxel was generally similar to that of docetaxel alone, and consistent with previously reported results for ganetespib. The most common adverse events (AEs), all grades, were neutropenia (42% vs. 43%), diarrhea (48% vs. 16%) and fatigue (34% vs. 24%), for G+D (N=123) vs. D (N=125), respectively. Diarrhea was effectively managed with supportive care; the incidence of grade 3 or 4 diarrhea was 3% (G+D) vs. 0% (D). Fatigue was predominantly grade 1 and grade 2; grade 3 or 4 fatigue was 6% (G+D) vs. 3% (D). The most common grade 3 or 4 AEs were neutropenia (37% vs. 38%), febrile neutropenia (11% vs. 2%), and anemia (8% vs. 2%). The proportions of patients with AEs leading to death were 12% vs. 11%, and AEs leading to treatment discontinuation were 7% vs. 5% for G+D vs. D, respectively.

Consistent with prior findings with ganetespib, reports of visual impairment in this study were infrequent: 2 (2%) in the G+D arm and 0 (0%) in the D arm. Both cases of visual impairment were transient and grade 1 or 2. A high incidence of visual impairment has been reported following treatment with certain other Hsp90 inhibitors.

Investor meeting and webcast

Synta will host a presentation for investors on June 3, 2013 at 7:00 PM CDT, to discuss these results. The live webcast and replay of the presentation will be available on the home page and in the Investors section of the Synta 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, 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 over 20 clinical trials including trials in lung, breast, colorectal, and hematologic malignancies. Information on these trials can be found at www.clinicaltrials.gov.

About the GALAXY Program

The GALAXY (Ganetespib Assessment in Lung cAncer with docetaXel) program consists of two randomized trials comparing the combination of ganetespib and docetaxel versus docetaxel alone in patients with Stage IIIB/IV NSCLC who have received one prior systemic therapy: a 300-patient Phase 2b/3 trial (GALAXY-1) to determine the patient population most likely to derive benefit from

ganetespib, and a 500-patient confirmatory Phase 3 trial (GALAXY-2). More information about the GALAXY trials can be found at www.clinicaltrials.gov (NCT01348126 and NCT01798485).

About Lung Cancer

Lung cancer is the leading cause of cancer-related death in the world, accounting for nearly 1.4 million deaths in 2008, according to the World Health Organization. The five-year survival rate for this disease is approximately 16%; over half of people with lung cancer die within one year of being diagnosed. In the U.S., the American Cancer Society estimates that 228,000 cases of lung cancer will be diagnosed in 2013. Non-small cell adenocarcinoma comprises about 40% of all lung cancer.

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

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 the expected timing, developments and progress of the GALAXY trials and to the potential for ganetespib plus docetaxel to be the first combination therapy for second-line treatment of adenocarcinoma of the lung 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.

References

1. Tsutsumi S, Beebe K, Neckers L. Impact of heat-shock protein 90 on cancer metastasis. Future Oncol. 2009 Jun;5(5):679-88.
2. Staufer K, Stoeltzing O. Implication of heat shock protein 90 (HSP90) in tumor angiogenesis: a molecular target for anti-angiogenic therapy? Curr Cancer Drug Targets. 2010 Dec;10(8):890-7.
3. Li W et al. Secreted Hsp90 is a novel regulator of the epithelial to mesenchymal transition (EMT) in prostate cancer. J Biol Chem. 2012 Nov 2;287(45):37732-44
4. Wang J et al. High expression of heat shock protein 90 is associated with tumor aggressiveness and poor prognosis in patients with advanced gastric cancer. PLoS One. 2013 Apr 26;8(4):e62876

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