Synta Reports on Progress with Lead HDC Compounds at IASLC Conference

February 24, 2014

- Results from two lead Hsp90-inhibitor Drug Conjugates, HDC SN-38 and HDC docetaxel, presented -

LEXINGTON, Mass.--(BUSINESS WIRE)--Feb. 24, 2014-- Synta Pharmaceuticals Corp. (NASDAQ:SNTA) today reported on progress with lead compounds from its Hsp90-Inhibitor Drug Conjugate (HDC) platform at the IASLC 14th Annual Targeted Therapies of the Treatment of Lung Cancer Meeting in Santa Monica, California. The new compounds, consisting of an Hsp90-inhibitor conjugated with SN-38 (HDC SN-38) and an Hsp90-inhibitor conjugated with docetaxel (HDC docetaxel), demonstrated proof of principle in multiple preclinical cancer models. Notably, complete or near complete regressions of tumors were observed in models of non-small cell lung cancer, small-cell lung cancer, breast cancer, pancreatic cancer, colon cancer, and skin cancer, in models that are generally resistant or show limited response to treatment with the unconjugated chemotherapies.

Results were presented by Dr. David Gerber of UT Southwestern Medical Center. “Synta’s HDC platform represents an exciting advancement in the field of tumor-targeted delivery,” said Dr. Gerber. “The therapeutic profile of any anti-cancer agent that can be chemically linked to an Hsp90 inhibitor could potentially be enhanced.”

“The HDC concept is very appealing and has potential to be an important new category of targeted therapy,” stated Dr. David Gandara, Director Thoracic Oncology Program, U.C. Davis Comprehensive Cancer Center, and Chair Lung Cancer Committee of the Southwest Oncology Group (SWOG). “HDCs may be the future of chemotherapy.”

HDCs are small-molecule drugs consisting of an Hsp90 inhibitor (targeting moiety) joined to an anti-cancer agent (payload) via a cleavable chemical linker optimized for controlled release of payload drug inside cancer cells. They exploit the preferential retention of Hsp90 inhibitors in tumors, which has been demonstrated both in preclinical models with a broad range of Hps90 inhibitors, and in patients in a recent clinical trial that used a radiolabeled Hsp90 inhibitor for PET (positron emission tomography). Imaging showed high concentration and prolonged retention of the Hsp90 inhibitor in patients’ tumors.

Other tumor-targeting strategies, such as antibody-drug conjugates (ADCs), consist of large proteins complexed with chemotherapy (molecular weight > 100,000) that require binding to a unique target on the cell surface, followed by endocytosis to deliver the protein complex through the cell membrane. The process generally requires the use ultra-potent payload toxins due to the complexity of the absorption process. In contrast, HDCs are small molecule drug conjugates (molecular weight < 1,000) that enter cells through passive diffusion or other small molecule uptake mechanisms, binding to the overexpressed Hsp90 inside the cancer cell. This simpler absorption allows higher achieved concentration, broader choice of anti-cancer payloads, and sustained, slow-release of the cytotoxic payload within the tumor.

Selective retention of HDCs by cancer cells enables a substantial increase in the amount of anti-cancer payload that can be delivered. Results presented at the conference showed that up to seven times greater dosage of docetaxel may be safely administered in the animal models compared to unconjugated docetaxel. This increase was associated with near complete regressions in animals treated with the HDC vs. limited activity or progressive disease in animals treated with unconjugated docetaxel. Preclinical safety results to date show comparable or more favorable safety profile of the HDC as compared with the unconjugated chemotherapy.

In addition, both the SN-38 and docetaxel HDCs demonstrated prolonged anti-tumor activity following the last dose of the HDC. These results are consistent with retention of the HDC in tumors and sustained, slow release of the cytotoxic payload within the tumor.

Dr. Weiwen Ying of Synta will be presenting additional results from Synta HDC studies at the Applied Pharmaceutical Chemistry 2014 Conference in Cambridge, Massachusetts on March 4.

Slides presented at the IASLC meeting are available at www.syntapharma.com

About Hsp90-Inhibitor Drug Conjugates (HDCs)

HDCs are small-molecule drugs consisting of an Hsp90 inhibitor (targeting moiety) joined to an anti-cancer agent (payload) via a cleavable chemical linker optimized for controlled release of payload drug inside cancer cells. They exploit the preferential retention of Hsp90 inhibitors in tumors to selectively deliver anti-cancer payloads. HDCs represent a promising new therapeutic class with the potential to enhance the safety and efficacy of a wide range of small molecule anti-cancer drugs.

Synta has established proof of concept for HDC lead candidates in preclinical studies and has developed over 450 compounds, using a broad range of Hsp90 inhibitor moieties, cleavable linkers, and anti-cancer payloads. The latter include cytotoxic chemotherapeutics, kinase inhibitors, hormone therapies, immunomodulators, and epigenetic modifiers, creating the potential for next-generation compounds in each of these categories. Synta has filed worldwide patent applications that include comprehensive claims covering the HDC platform, compositions of matter, methods for identifying therapeutically effective compounds, and methods of use of such compounds against a wide range of diseases and conditions.

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 potential for enhancing the therapeutic profile of anti-cancer agents using Synta's HDC platform, 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.

Source: Synta Pharmaceuticals Corp.

Investors:
Synta Pharmaceuticals Corp.
Mindy Kohl, 781-541-7213
mkohl@syntapharma.com
or
Argot Partners
Andrea Rabney, 212-600-1494
andrea@argotpartners.com
or
Media:
Argot Partners
Eliza Schleifstein, 917-763-8106
eliza@argotpartners.com