Syndax Pharmaceuticals Announces Publication of Clinical Study Demonstrating that Entinostat Targets Resistance Pathways in Breast Cancer

--Results Published in Journal of Clinical Oncology Show for the First Time that Adding Entinostat to Antiestrogen Therapy May Be an Effective Approach to Targeting Resistance Pathways in Breast Cancer--

Waltham, Mass.-- May 14, 2013-- Syndax Pharmaceuticals, Inc., a late-stage oncology company focused on developing novel combination epigenetic strategies to treat cancers that have become resistant to standard treatments, announced today the publication in the ***Journal of Clinical Oncology*** of positive results of a phase 2 randomized, double-blind, placebo-controlled study of the company's lead drug entinostat. The study showed that entinostat extended both progression-free survival and overall survival when added to exemestane in postmenopausal women with estrogen receptor-positive (ER+) breast cancer whose cancer had progressed after treatment with a nonsteroidal aromatase inhibitor.

"These remarkable results show that adding entinostat, a class I histone deacetylase inhibitor (HDAC) to standard antiestrogen therapy may be an effective, well tolerated approach to targeting resistance pathways in breast cancer, particularly in hormone-positive disease," said lead author Denise A. Yardley, M.D., Senior Investigator, Sarah Cannon Research Institute; Associate, Tennessee Oncology, PLLC. "Additionally, for the first time, we identified a potential biomarker in a subset of patients with estrogen receptor positive tumors that was associated with a greater progression-free survival, which may ultimately offer the potential for improved clinical outcomes with entinostat."

The study evaluated entinostat in 130 postmenopausal women with advanced ER+ breast cancer, progressing on a nonsteroidal aromatase inhibitor. Patients were randomly assigned to 25 mg exemestane daily plus 5 mg entinostat once per week (64 patients), or exemestane plus placebo (66 patients). The primary end point was

progression-free survival (PFS); blood was also collected in a subset of patients for evaluation of protein lysine acetylation as a biomarker of entinostat activity.

Based on intent-to-treat analysis, patients treated with entinostat saw improved median PFS to 4.3 months, versus 2.3 months in patients treated with placebo (hazard ratio 0.73; 95% confidence interval, 0.50 to 1.07; one-sided P = .055; two-sided P = .11). Overall survival was an exploratory endpoint, and median survival improved to 28.1 months in entinostat-treated patients versus 19.8 months in placebo-treated (hazard ratio 0.59; 95% confidence interval, 0.36 to 0.97; P = .036). Fatigue and neutropenia were the most frequent grade 3/4 toxicities; treatment discontinuation because of adverse events was higher in the entinostat group versus the placebo group (11 percent versus 2 percent). Protein lysine hyperacetylation in the entinostat-treated biomarker subset was associated with prolonged progression-free survival.

“Given the need for well tolerated therapies that extend the benefit of hormone therapy in postmenopausal women with breast cancer, our ENCORE 301 study supports the evaluation of entinostat not just in breast cancer, but also in other solid tumors,” said Arlene M. Morris, Syndax’s chief executive officer. “We are actively working to move entinostat into a confirmatory pivotal study this fall.”

In addition to the breast cancer study publication Syndax just announced a license deal to commercialize a first-in-class lung cancer treatment strategy with entinostat in combination with erlotinib developed by the University of Colorado and based on results published in Journal of Clinical Oncology in 2012. Click **here** to see the release.

About Entinostat for Breast Cancer

Each year, approximately 207,000 women in the United States have breast cancer; 20,000 of these women have metastatic breast cancer, which has spread to other parts of the body. About 70 percent of women with breast cancer have estrogen receptor-positive (ER+) breast cancer. For most of these patients, blocking estrogen activity with aromatase inhibitors represents an effective treatment. However, some women’s cancers may develop a resistance to aromatase inhibitors, leading to further disease progression requiring more toxic, less effective chemotherapies.

Delaying drug resistance and disease progression represents a significant unmet need, which if addressed could prolong survival, while decreasing the substantial health care costs associated with chemotherapy and hospitalization. Prior studies have shown that resistance to aromatase inhibitors develops due to increased activity in growth factor

signaling pathways, and decreased levels of estrogen receptor-alpha (ERα). Entinostat effectively decreases growth factor signaling in breast cancer cells where these pathways are active, and increases the estrogen receptor expression in breast cancer cells that might have negligible or undetectable levels of ERα.

Entinostat's proven ability to target multiple mechanisms of resistance establishes it as a promising candidate for preventing and overcoming aromatase inhibitor resistance through epigenetic modulation. In pre-clinical testing entinostat induced tumor regression when combined with an aromatase inhibitor after the development of hormone resistance, supported by a subsequent phase 2 trial ENCORE 303 in metastatic ER+ breast cancer patients progressing on treatment with aromatase inhibitors. Additional research is currently underway, in collaboration with the National Cancer Institute, to evaluate entinostat in triple-negative breast cancer.

About Syndax Pharmaceuticals

Syndax is a late-stage oncology company initiating pivotal programs in solid tumors based on employing epigenetic strategies to overcome the problem of resistance in oncology care. Syndax holds worldwide rights to entinostat, an oral, highly selective histone deacetylase (HDAC) inhibitor being developed in advanced breast and lung cancer. Randomized, placebo-controlled phase 2 studies with entinostat have demonstrated promising results in combination with aromatase inhibitors in breast cancer (ENCORE 301) and with the EGFR-TKI erlotinib (ENCORE 401) in non-small cell lung cancer providing the basis for moving entinostat into pivotal, phase 3 testing across a platform of solid tumor indications. NCI and Syndax are collaborating on the development of entinostat under a Cooperative Research and Development Agreement. The company is supported by top venture capitalists and led by industry experts developing treatments for large markets including metastatic breast and lung cancer. Formed in 2005, Syndax's intellectual property is based on work from scientific founder Ronald Evans, Ph.D., recipient of the 2004 Albert Lasker Prize for Basic Medical Research, a Member of the National Academy of Sciences, a professor at the Salk Institute for Biological Studies and a Howard Hughes Medical Institute Investigator. For more information please visit www.syndax.com.

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