



Syndax Pharmaceutical's Positive Phase 2 Data Supports Potential for Entinostat in Advanced Breast Cancer

**-- Entinostat in combination with exemestane prolonged progression-free survival --
-- Randomized, placebo-controlled data to be in an oral presentation at ASCO Breast Cancer Symposium 2011 --**

Waltham, Mass. – Sept. 6, 2011 – [Syndax Pharmaceuticals, Inc.](http://www.syndaxpharm.com), a clinical-stage epigenetics oncology company, announced today that ENCORE 301, a randomized, placebo-controlled phase 2 study of exemestane with and without entinostat hit its primary endpoint of an improvement in progression-free survival (PFS). The study showed that patients who received entinostat, a novel, oral small molecule inhibitor of class I histone deacetylases, with the hormone therapy exemestane, lived longer without their disease getting worse than people who received exemestane alone. Safety and efficacy results from the trial will be presented in a poster and an oral presentation at the American Society of Clinical Oncology (ASCO) Breast Cancer Symposium 2011 in San Francisco, CA this week.

“Entinostat combined with exemestane prolonged progression-free survival, reducing the risk of disease progression by 27% and showing an improvement in overall survival for post-menopausal women with estrogen-receptor positive metastatic breast cancer,” said Denise A. Yardley, MD, breast program leader, senior investigator at the Sarah Cannon Research Institute and principal investigator of the study. “Furthermore, in a subset of patients evaluated for a pharmacodynamic measure of entinostat’s effect, we demonstrated for the first time with this class of agents evidence of an association of protein lysine hyperacetylation with clinical outcome. I am extremely excited to be able to work with Syndax to validate the findings from this randomized phase 2 blinded, placebo-controlled trial with the development of a larger phase 3 confirmatory trial in hormone receptor-positive advanced breast cancer patients.”

ENCORE 301 (ENTinostat Combinations Overcoming RESistance) was a multicenter, randomized, double-blind, placebo-controlled, phase 2 study of exemestane with and without entinostat in 130 postmenopausal women with locally recurrent or metastatic estrogen receptor-positive breast cancer, progressing on treatment with the non-steroidal aromatase inhibitors anastrozole or letrozole. The primary endpoint of the study was progression-free survival. Other endpoints included objective response rate (ORR), clinical benefit rate (CBR), overall survival (OS) and safety and tolerability. All patients had received prior hormonal therapy (1 prior line 42%; >1 prior line 58%), and 33% had received prior chemotherapy in the advanced breast cancer setting. The results of this study with well-balanced arms included the following:

- In the intent-to-treat population progression-free survival was significantly longer (defined prospectively as 1-sided $p < 0.10$) with exemestane plus entinostat than with exemestane plus placebo (4.28 versus 2.27 months, respectively; hazard ratio (HR) = 0.73; $p = 0.06$);
- In the intent-to-treat population, with a median follow-up of 18 months, overall survival was significantly longer with exemestane plus entinostat than with exemestane plus placebo (26.94 versus 20.33 months, respectively; hazard ratio (HR) = 0.56; $p = 0.027$);
- In the subset of entinostat patients with protein acetylation data ($n = 27$), median PFS increased to over six months in the patients exhibiting protein lysine hyperacetylation;
- Entinostat combined with exemestane was well tolerated with the most frequent adverse events (AE) consisting of fatigue, gastrointestinal disturbances and hematologic abnormalities; and

- Serious AE rate was similar for exemestane plus entinostat (13%) and exemestane plus placebo (12%).

“Delaying disease progression and improving survival, combined with an attractive safety profile, makes entinostat and exemestane an exciting option for patients with advanced ER-positive breast cancer,” said Kathy D. Miller, MD, associate professor at Indiana University and trial investigator. “Hormone therapy remains the mainstay of treatment for patients with hormone-sensitive disease. These clinical results provide hope to clinicians and patients that we may be able to delay resistance and increase the time to disease progression, maintaining women longer on hormone-based therapy with fewer side effects than chemotherapy.”

ENCORE 301 data will be presented in a poster session on Friday, September 9 from 4:30 to 5:45 PM PT and during an oral session on Saturday, September 10 from 10:00 to 11:30 AM PT in San Francisco, CA during the ASCO Breast Cancer Symposium 2011.

“Based on the positive results from ENCORE 301 and the enthusiasm of the breast cancer community, we plan to enroll the first patient into a global, pivotal phase 3 study in early 2012,” said Joanna Horobin, MD, president and chief executive officer of Syndax. “While epigenetic drugs are approved for hematologic malignancies, if entinostat proves successful in this breast cancer setting, this would be the first epigenetic therapy to benefit patients with solid tumors, representing not only an important contribution to the treatment of breast cancer but a significant commercial opportunity.”

Breast Cancer and Hormone Therapy

Approximately 230,000 new cases of invasive breast cancer are diagnosed in women annually in the United States and there are approximately 150,000 women living with metastatic breast cancer (MBC). Over 70 percent of women with breast cancer have estrogen receptor-positive (ER+) breast cancer. The most effective cancer treatments target the underlying biology and in breast cancer the most common oncogenic driver is estrogen receptor signaling. Blocking estrogen activity with aromatase inhibitors represents an effective treatment for most ER+ MBC patients, however acquired drug resistance to aromatase inhibitors leads to disease progression, ultimately requiring less effective, more toxic chemotherapies.¹ Delaying resistance and disease progression represents a significant unmet need that could prolong survival while decreasing health care costs associated with chemotherapy and hospitalization.

About Entinostat

Syndax’s lead product entinostat is a novel, oral small molecule inhibitor of class I histone deacetylases, key enzymes that alter the structure of chromatin to control gene expression. Entinostat is differentiated from other members of the class through its unique selectivity profile, pharmacokinetic properties and safety profile. Entinostat has been studied in more than 600 cancer patients where objective tumor responses have been observed in both solid and hematologic malignancies. Breast cancer animal models demonstrated that resistance to aromatase inhibitors occurs through up-regulation of growth factor signaling pathways and down-regulation of estrogen receptor alpha. Entinostat effectively down-regulates growth factor signaling in breast cancer cells where these pathways are active. Entinostat also up-regulates the expression of ER in breast cancer cells which have negligible or undetectable levels of estrogen receptor. The ability to target multiple mechanisms of resistance establishes entinostat 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 aromatase inhibitors after the development of aromatase inhibitor resistance.

Additional [phase 2 studies](#) with entinostat have demonstrated promising results in combination with the EGFR-TKI erlotinb (ENCORE 401) in non-small cell lung cancer and as a single agent in Hodgkin's lymphoma (ENGAGE 501). Results from the ENCORE clinical program provide the basis for moving entinostat into pivotal, phase 3 testing in metastatic breast and lung cancer settings.

About Syndax

Syndax Pharmaceuticals, Inc. is a Waltham, MA-based, late-stage, oncology-focused pharmaceutical company. Syndax is building a portfolio of new oncology products to extend and improve the lives of patients by developing and commercializing novel cancer therapies in optimized, mechanistically driven combination regimens. Formed in 2005, the company'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. Syndax has worldwide rights to develop and commercialize entinostat and is backed by top-tier Venture Capital firms: Domain Associates, MPM Capital, Avalon, Pappas and Forward Ventures. For more information please visit www.syndax.com.

Contact Information

E. Blair Schoeb
Syndax Pharmaceuticals, Inc
Tel: 908-277-0386
bschoeb@syndax.com

1. Hurvitz, S, Pietras, R. Rational Management of Endocrine Resistance in Breast Cancer, *Cancer*, 2385- 2397 (2008).

###