



ABSTRACT #567

Syndax Pharmaceuticals to Present Updated Overall Survival Data With Entinostat in Metastatic Breast Cancer at ASCO

-- At two-year follow-up, entinostat plus exemestane demonstrates continued survival benefit --
-- Entinostat to enter phase 3 based on positive phase 2 randomized, placebo controlled results--

Waltham, Mass. – May 29, 2012 – Syndax Pharmaceuticals, Inc., a late-stage oncology company, announced today that updated results from ENCORE 301, a randomized, placebo-controlled phase 2 study of exemestane with and without entinostat in estrogen receptor positive metastatic breast cancer demonstrated improvement in overall survival for patients treated with exemestane plus entinostat. At median follow up of 25 months, treatment with the combination resulted in an 8.3 months improvement in overall survival (an exploratory endpoint) corresponding to a 41% reduction in the risk of dying ($p = 0.04$). Updated safety and efficacy results from the trial will be presented in a poster session at the [American Society of Clinical Oncology](#) (ASCO) annual meeting in Chicago, IL on Saturday, June 2, 2012.

Previously [reported results](#) indicated the study met the designated primary endpoint of progression-free survival (PFS) (4.28 versus 2.27 months, respectively; hazard ratio (HR) = 0.73; $p=0.06$). Additionally, in the subset of patients assessed for the pharmacodynamic marker of protein lysine acetylation in peripheral blood cells, acetylation in entinostat-treated patients was associated with prolonged progression-free survival to over six months across all peripheral mononuclear cell types analyzed.

“Entinostat combined with exemestane extends the lives of post-menopausal women with estrogen-receptor positive MBC as compared to those women that received exemestane combined with placebo and ongoing analyses of the data has not identified any contributing factors beyond the potential contribution of entinostat to account for the extended overall survival benefit,” said Denise A. Yardley, MD, breast program leader, senior investigator at the Sarah Cannon Research Institute and principal investigator of the study. “Moreover, the addition of entinostat to exemestane translated into an increase in progression-free survival of over six months in the subset of patients treated with this novel combination that demonstrated protein lysine hyperacetylation. This suggests that evaluating evidence of protein hyperacetylation may be an exciting opportunity to explore whether we could use this biomarker to identify patients most likely to benefit from the addition of entinostat to standard hormone therapy. These results continue to support the promise of entinostat for women with advanced breast cancer and I am eager to move forward with the confirmatory phase 3 study.”

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 post-menopausal women with locally recurrent or metastatic estrogen receptor-positive breast cancer, progressing on treatment with the non-steroidal aromatase inhibitors anastrozole or letrozole. The study hit the primary endpoint of progression-free survival and preliminary analysis indicated an overall survival benefit. Entinostat was well tolerated with fatigue, nausea and uncomplicated neutropenia as the most commonly occurring adverse events. Pharmacodynamic analysis in a subset of patients linked for the first time a readout of histone deacetylase inhibitor activity with clinical outcome.

The abstract titled, “Characterization of the overall survival benefit in ENCORE 301, a randomized placebo-controlled phase 2 study of exemestane with and without entinostat in ER+ post-menopausal women with metastatic breast cancer” highlighted the following results:

- Analysis of OS across multiple subsets of interest demonstrated a consistent benefit in the exemestane and entinostat (EE) group versus exemestane and placebo (EP);
- Sensitivity analysis of baseline characteristics potentially impacting OS did not identify any factors that influenced the effect of EE on OS;
- Examination of treatments received during follow-up after discontinuation of EE and EP demonstrated balance between treatment group for patients receiving chemotherapy (48% EE: 44% EP), hormone therapy (37% EE: 35% EP), bisphosphonates (2% EE; 0% EP), radiation (6% EE; 5%EP), and surgery (0% EE: 2% EP);
- Compared to EP, OS was longer in EE group for patients whose first subsequent treatment was a hormone therapy (EE median not reached vs EP median 20.5 months; HR 0.65 [95% CI 0.26, 1.58]) or chemotherapy (EE median 26.9 months vs EP median 17.6 months; HR 0.51 [95% CI 0.25, 1.04])

“The metastatic breast cancer community needs new treatment options that can improve survival,” said Joanna Horobin, MD, president of Syndax. “We are hopeful that the positive data we have seen so far in the randomized, phase 2 clinical trial will be confirmed in the phase 3 study. If positive, entinostat would be the first epigenetic therapy to benefit patients with solid tumors, representing not only an important new treatment option for women with ER positive MBC but a significant commercial opportunity for Syndax.”

In addition to the breast cancer data, an abstract highlighting the immunomodulatory effects of entinostat entitled, “Phase I/II study of high-dose interleukin 2, aldesleukin, in combination with the histone deacetylase inhibitor entinostat in patients with metastatic renal cell carcinoma” will be presented in a poster session on Sunday, June 3 from 8:00 AM to 12:00 PM CT.

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. 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 700 cancer patients where objective tumor responses have been observed in both solid and hematologic malignancies. Preclinical studies have demonstrated that entinostat can overcome resistance to a wide variety of targeted

therapies including hormone therapy, receptor tyrosine kinase inhibitors, and chemotherapy.

Additional [phase 2 studies](#) with entinostat have demonstrated promising results in combination with the EGFR-TKI erlotinib (ENCORE 401) in non-small cell lung cancer (NSCLC), in combination with the DNA methyltransferase inhibitor azacitidine in NSCLC 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 complemented by biomarker driven confirmatory studies in lung cancer.

About Syndax

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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