Entinostat Improves Treatment Outcomes When Combined with Immune Checkpoint Blockade in Preclinical Tumor Models

Studies Support Ongoing Clinical Strategy of Using Syndax's Entinostat as Epigenetic Priming to Immune Therapy

WALTHAM, Mass.- July 30, 2014 – Syndax Pharmaceuticals, Inc. today announced that newly published results demonstrate that in preclinical studies entinostat significantly improved treatment outcomes in mouse tumor models when combined with anti-PD1 and anti-CTLA4 targeted antibodies. The paper from Kim, et al. at The Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine, titled "Eradication of metastatic mouse cancers resistant to immune checkpoint blockade by suppression of myeloid derived cells" was published in the journal Proceedings of the National Academy of Sciences (PNAS). The study demonstrated that the combination therapy produced 100 percent inhibition of primary tumors and metastases in aggressive mouse colorectal and breast tumor models. The authors also reported an 80 percent cure rate when epigenetic therapy with entinostat and azacitidine was combined with anti-PD1 and anti-CTLA4 antibodies in an aggressive non-immunogenic metastatic breast cancer mouse model.

The mechanism underlying these results, the authors note, is believed to be entinostat's inhibition of myeloid derived suppressor cells (MDSCs) at concentrations which importantly have only modest effects on CD8+ T cells creating the potential for a large therapeutic window in which MDSCs can be depleted while sparing CD8+ T cells.

"We now have strong pre-clinical and anecdotal clinical data that provide potential evidence of entinostat's immuno-modulatory activity and potential immune-priming effects to anti-cancer immune therapies," said Peter Ordentlich, Ph.D., co-founder and chief technology officer of Syndax. "These new results, which are consistent with earlier data demonstrating entinostat inhibition of regulatory T cells, show that epigenetic therapy with entinostat may increase immunogenicity of tumors and reduce resistance to immune therapy through potent inhibition of host immune suppressor cells."

Arlene Morris, chief executive officer of Syndax added, "We expect additional validation for entinostat's immune-modulatory activity from ongoing clinical trials including a Phase 2 study evaluating epigenetic priming to the PD-1 blocker nivolumab in non-small cell lung cancer and a Phase 2 study of entinostat in combination with aldesleukin (IL-2) in patients with advanced renal cell cancer. Additional studies of entinostat in combination with anti-PD1/PDL1 therapy are planned. These recent findings highlight promising new

opportunities for entinostat that complement the ongoing pivotal Phase 3 study testing entinostat's ability to reverse resistance to hormone therapy in men and women with metastatic estrogen receptor positive (ER+) breast cancer."

Syndax did not provide any financial support for the study reported in this paper.

**Reference: KiBem Kim, Andrew D. Skora, Zhaobo Li, Qiang Liu, Ada J. Tam, Richard L. Blosser, Luis A. Diaz, Jr., Nickolas Papadopoulos, Kenneth W. Kinzler, Bert Vogelstein and Shibin Zhou. Eradication of metastatic mouse cancers resistant to immune checkpoint blockade by suppression of myeloid derived cells. Proc Natl Acad Sci, Published online before print on July 28, 2014.

Syndax Pharmaceuticals

Syndax is developing entinostat for the treatment of patients with therapy-resistant cancers. Entinostat is being developed to target resistance to current cancer therapies through an epigenetic mechanism and has been designated a Breakthrough Therapy by the FDA when used in combination with exemestane in HR+ advanced (locally advanced or metastatic) breast cancer. Entinostat is an oral, selective HDAC inhibitor that is being evaluated in combination with exemestane in a pivotal Phase 3 clinical study for the treatment of hormone receptor-positive metastatic breast cancer. Syndax holds rights to entinostat in all major markets.

Cautionary Note on Forward-Looking Statements

This press release contains forward-looking statements. Forward-looking statements contained in this press release include statements about the results of the preclinical studies and entinostat's potential immuno-modulatory activity and potential immune-priming effects suggested by these results, as well as the Company's plan for additional clinincal trials and potential validation from future trials. Words such as "may," "believe," "will," "expect," "plan," "anticipate," "estimate," "intend" and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify forward-looking statements. These forward-looking statements are not guarantees of future performance and involve a number of unknown risks, assumptions, uncertainties and factors that are beyond Syndax's control. All forward-looking statements are based on Syndax's expectations and assumptions as of the date of this press release. Actual results may differ materially from these forward-looking statements. Except as required by law, Syndax expressly disclaims any responsibility to update any forward-looking statement contained herein, whether as a result of new information, future events or otherwise.