Syndax's Entinostat Receives Breakthrough Therapy Designation from FDA for Treatment of Advanced Breast Cancer

Epigenetic Mechanism with Potential to Reverse Resistance to Hormonal Therapy in Patients with Limited Treatment Options

WALTHAM, Mass., Sept. 11, 2013—Syndax Pharmaceuticals Inc. today announced that the U.S. Food and Drug Administration (FDA) has designated entinostat as a Breakthrough Therapy for the treatment of locally recurrent or metastatic estrogen receptor-positive (ER+) breast cancer when added to exemestane in postmenopausal women whose disease has progressed following non-steroidal aromatase inhibitor therapy. Entinostat is an investigational histone deacetylase inhibitor (HDACi) set to begin Phase 3 testing in combination with exemestane in postmenopausal women with metastatic ER+ breast cancer who have progressed on hormonal therapy.

The Breakthrough Therapy designation for entinostat is based on data from the completed Phase 2 ENCORE 301 study, in which entinostat was shown to extend both progression-free survival and overall survival when added to exemestane in postmenopausal women with ER+ metastatic breast cancer whose cancer had progressed after treatment with a nonsteroidal aromatase inhibitor and with a very acceptable tolerability profile. A Phase 3 trial, planned to begin enrolling patients in the first quarter of 2014 is currently being developed by the ECOG-ACRIN Cancer Research Group, which would conduct the study under the sponsorship of the Division of Cancer Treatment and Diagnosis, National Cancer Institute (NCI).

"The FDA's decision to designate entinostat a Breakthrough Therapy is important validation of the drug's therapeutic potential in women with advanced breast cancer," said Arlene M. Morris, Syndax's chief executive officer. "Currently, women with ER+ breast cancer who have progressed on hormonal therapy have limited therapeutic options. Entinostat's epigenetic mechanism may reverse resistance to hormonal therapy, delaying the need for toxic chemotherapeutic agents and improving survival when given in combination with aromatase inhibitors. This breakthrough designation will allow us to more rapidly bring this new treatment option to patients who may benefit from its availability."

The Food and Drug Administration Safety and Innovation Act (FDASIA), signed in July, 2012, created the Breakthrough Therapy Designation. According to the FDA, the designation allows the expedited development and review of a drug to treat a serious or life threatening disease or condition intended alone or in combination with one or more other drugs for which preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints.[1]

About Entinostat

Entinostat, Syndax's lead product candidate, has been studied in more than 800 cancer patients where objective tumor responses have been observed in both solid and hematologic malignancies. Entinostat's established safety and efficacy profile as both a single agent and in combination with a number of commercially available targeted therapies differentiates it from

other histone deacetylase inhibitors(HDACi). Having demonstrated promising clinical results in breast and lung cancer, entinostat is moving toward pivotal clinical testing. It is an oral, novel inhibitor of class I histone deacetylases, key enzymes that alter the structure of chromatin to control gene expression. This aberrant gene expression can result in reversible, epigenetically-based drug tolerance. Designed to selectively target the HDAC isoforms most relevant to the biology of tumors, entinostat can normalize dysregulated gene expression in cancer cells, thereby restoring sensitivity to targeted therapy. Entinostat is the first HDACi with positive results in a randomized Phase 2 study in breast cancer and is the only HDACi in late-stage development for this indication.

About Syndax Pharmaceuticals

Syndax is focused on employing epigenetic strategies to overcome the problem of resistance in oncology care in solid tumors. The company holds worldwide rights to entinostat, an oral, highly selective histone deacetylase (HDAC) inhibitor in late-stage clinical development for the treatment of advanced breast cancer and lung cancer. A randomized, placebo-controlled Phase 2 study of entinostat in combination with aromatase inhibitors in breast cancer (ENCORE 301) demonstrated an improvement in both progression-free survival and overall survival, providing the basis for the evaluation of entinostat in pivotal Phase 3 testing in metastatic breast cancer. Entinostat also demonstrated promising results in a subset of non-small cell lung cancer patients when given in combination with the EGFR-TKI erlotinib (ENCORE 401). NCI and Syndax are collaborating on the development of entinostat under a Cooperative Research and Development Agreement aimed at improving survival in advanced, hard-to-treat cancers.

For more information, visit www.syndax.com.

1. U.S. Food and Drug Administration. Frequently Asked Questions: Breakthrough Therapies. 2013. http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/SignificantAmendmentstotheFDCAct/FDASIA/ucm341027.htm. Accessed April 19, 2013.

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