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Preclinical Results Support Entinostat's Role in Targeting the Tumor Microenvironment to Enhance Immune Checkpoint Therapy

-Results Published Online in Clinical Cancer Research Show Entinostat Inhibits Function of Myeloid Derived Suppressor Cells Resulting in Enhanced Antitumor Effect in Murine Models of Lung and Renal Cell Carcinoma-

WALTHAM, Mass. and PHILADELPHIA and INDIANAPOLIS, July 11 2017 /PRNewswire/ -- Syndax Pharmaceuticals, Inc. ("Syndax," the "Company" or "we") (Nasdaq:SNDX), a clinical stage biopharmaceutical company developing entinostat and SNDX-6352 in multiple cancer indications, in collaboration with The Wistar Institute and Indiana University Melvin and Bren Simon Cancer Center, today announced the publication of a preclinical report demonstrating that entinostat, Syndax's oral, Class-I histone deacetylase inhibitor, enhances the antitumor effect of PD-1 (programmed death receptor-1) blockade through the inhibition of myeloid derived suppressor cells (MDSCs).

The article, titled "Entinostat Neutralizes Myeloid Derived Suppressor Cells and Enhances the Antitumor Effect of PD-1 Inhibition in Murine Models of Lung and Renal Cell Carcinoma," was published in *Clinical Cancer Research* and is available [online](#).

Researchers tested the effect of combining entinostat with an anti-PD-1 monoclonal antibody that enhances the T cell-mediated antitumor immune response. The studies were conducted in two mouse models of renal cell carcinoma and lung cancer and included a series of *in vitro* experiments aimed at characterizing the effects of this combined treatment on the myeloid derived suppressor cells (MDSCs), a highly immunosuppressive population of tumor infiltrating immature myeloid cells. The results indicated that entinostat has an inhibitory effect on MDSC immunosuppressive function both *in vivo* and *in vitro*, which results in enhanced anti-tumor activity of the combination.

"The use of PD-1 inhibitors in the treatment of solid tumors has demonstrated significant benefit, but many patients still present with progressive disease following treatment," said co-lead researcher Dmitry I. Gabrilovich, M.D., Ph.D., Professor and Program Leader, Translational Tumor Immunology Program, The Wistar Institute. "We have previously demonstrated the role of MDSCs as important mediators of resistance to immune therapy approaches. The results from our new study suggest that entinostat may enhance the anti-tumor efficacy of PD-1 targeted therapy through MDSC targeting, potentially providing an effective combination treatment approach for patients with solid tumors, including lung and renal cell carcinoma."

"Our group has previously reported that entinostat enhances the antitumor effect of high dose interleukin 2 in renal cell carcinoma both in mice and patients. These new findings confirm that the combination of entinostat with immunotherapy has significant immunomodulatory activity and may offer increased benefit for a larger population of patients with renal cell carcinoma, non-small cell lung cancer and other solid tumors with an immunosuppressive tumor microenvironment," said co-lead researcher Roberto Pili, M.D., Robert Wallace Miller Professor of Oncology and Professor of Medicine and Urology at IU Simon Cancer Center. "We are pleased to have obtained the same results in two different laboratories and we look forward to translating these preclinical findings into combination approaches with entinostat to enhance the clinical activity of immune checkpoint inhibition."

"We are excited that these current data support and extend initial observations generated at Johns Hopkins," said Peter Ordentlich, Ph.D., Chief Scientific Officer of Syndax. "Entinostat has now been shown to impact MDSCs in multiple preclinical tumor models across several laboratories as well as from blood samples taken from entinostat treated patients. These data collectively provide strong rationale for combining entinostat with immunotherapies for the treatment of solid tumors. We look forward to providing additional updates from the entinostat clinical development program."

About Syndax Pharmaceuticals, Inc.

Syndax is a clinical stage biopharmaceutical company developing an innovative pipeline of cancer therapies. Our lead product candidate, entinostat, which was granted Breakthrough Therapy designation by the FDA following positive results from our Phase 2b clinical trial, ENCORE 301, is currently being evaluated in a Phase 3 clinical trial for advanced hormone receptor positive, human epidermal growth factor receptor 2 negative breast cancer. Given its potential ability to block the function of immune suppressive cells in the tumor microenvironment, entinostat is also being evaluated in combination with approved PD-1 antagonists. Ongoing Phase 1b/2 clinical trials combine entinostat with KEYTRUDA[®] from Merck & Co., Inc.

for non-small cell lung cancer, melanoma and colorectal cancer; with TECENTRIQ[®] from Genentech, Inc. for triple negative breast cancer; and with BAVENCIO[®] from Pfizer Inc. and Merck KGaA, Darmstadt, Germany, for ovarian cancer. Our second product candidate, SNDX-6352, is a monoclonal antibody that blocks the CSF-1 receptor and may also block the function of immune suppressive cells in the tumor microenvironment. SNDX-6352 is being evaluated in a single ascending dose Phase 1 clinical trial and is expected to be developed to treat a variety of cancers.

Syndax's Cautionary Note on Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as "may," "will," "expect," "plan," "anticipate," "estimate," "intend," "believe" 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 based on Syndax's expectations and assumptions as of the date of this press release. Each of these forward-looking statements involves risks and uncertainties. Actual results may differ materially from these forward-looking statements. Forward-looking statements contained in this press release include, but are not limited to, statements about the progress, timing, clinical development and scope of clinical trials and the reporting of clinical data for Syndax's product candidates, and the potential use of our product candidates to treat various cancer indications. Many factors may cause differences between current expectations and actual results including unexpected safety or efficacy data observed during preclinical or clinical studies, clinical trial site activation or enrollment rates that are lower than expected, changes in expected or existing competition, changes in the regulatory environment, failure of Syndax's collaborators to support or advance collaborations or product candidates and unexpected litigation or other disputes. Other factors that may cause Syndax's actual results to differ from those expressed or implied in the forward-looking statements in this press release are discussed in Syndax's filings with the U.S. Securities and Exchange Commission, including the "Risk Factors" sections contained therein. Except as required by law, Syndax assumes no obligation to update any forward-looking statements contained herein to reflect any change in expectations, even as new information becomes available.

About The Wistar Institute

The Wistar Institute is an international leader in biomedical research with special expertise in cancer research and vaccine development. Founded in 1892 as the first independent nonprofit biomedical research institute in the country, Wistar has held the prestigious Cancer Center designation from the National Cancer Institute since 1972. The Institute works actively to ensure that research advances move from the laboratory to the clinic as quickly as possible. wistar.org.

About Indiana University Melvin and Bren Simon Cancer Center

The Indiana University Melvin and Bren Simon Cancer Center is the only National Cancer Institute-designated cancer center in Indiana that provides patient care. The NCI designation recognizes that its collaborative research programs meet the NCI's rigorous criteria for world-class, state-of-the-art programs in multidisciplinary cancer research. The mission of the IU Simon Cancer Center is to eliminate cancer's burden in Indiana and beyond. Cancer.iu.edu.

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View original content:<http://www.prnewswire.com/news-releases/preclinical-results-support-entinostat's-role-in-targeting-the-tumor-microenvironment-to-enhance-immune-checkpoint-therapy-300486457.html>

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