



Syndax Announces Updated Results from Phase 2 ENCORE 601 Trial of Entinostat in Combination with KEYTRUDA® (pembrolizumab)

May 17, 2018

- Ongoing ENCORE 601 biomarker analyses suggest enhanced clinical benefit in subpopulation of PD-(L)1 refractory NSCLC patients with high levels of peripheral blood monocytes; 29% ORR and 5.4 months PFS observed in subpopulation -
 - Potential registration pathway identified in NSCLC; next trial anticipated to commence by the end of 2018 -
- Clinical follow up and biomarker assessments ongoing in ENCORE 601 melanoma cohort; enrollment expanding in CRC cohort -
- Data announced today to be presented at upcoming ASCO Annual Meeting -
- Company to host conference call today at 8:30 a.m. ET -

WALTHAM, Mass., May 17, 2018 /PRNewswire/ -- Syndax Pharmaceuticals, Inc. ("Syndax," the "Company" or "we") (Nasdaq: SNDX), a clinical stage biopharmaceutical company developing an innovative pipeline of cancer therapies, today announced updated results from multiple cohorts of the ongoing Phase 2 ENCORE 601 trial of entinostat in combination with KEYTRUDA® (pembrolizumab), Merck's anti-PD-1 (programmed death receptor-1) therapy. This data will be presented at the American Society of Clinical Oncology (ASCO) Annual Meeting being held June 1-5, 2018 in Chicago, Illinois.

ENCORE 601 is a Phase 1b/2 trial evaluating the efficacy and safety of entinostat in combination with pembrolizumab across multiple cohorts of PD-(L)1 treatment-naïve and pre-treated cancers, including non-small cell lung cancer (NSCLC), melanoma and microsatellite stable colorectal cancer (MSS-CRC). Confirmed objective responses with the combination regimen have been observed across all cohorts. Updated data continue to demonstrate a manageable toxicity profile for the entinostat-pembrolizumab combination, with treatment emergent adverse events observed consistent with those previously reported. The ENCORE 601 study also incorporates an extensive biomarker assessment of pre- and on-treatment blood and tumor samples from all patient cohorts with the goal of identifying a patient enrichment strategy that may predict enhanced clinical benefit across various cohorts and, therefore, potentially inform the design of future registration-directed studies.

"The additional data from the ENCORE 601 program continue to support the potential for the entinostat-pembrolizumab combination to serve as an effective therapeutic option across a variety of indications," said Briggs Morrison, M.D., Chief Executive Officer of Syndax. "We are especially pleased to be able to share preliminary findings from our efforts to identify biomarkers that could aid in predicting which patients may derive a clinical benefit from this combination therapy. We have now identified a potential registration pathway in NSCLC and look forward to providing further updates as our plans come together."

NSCLC Update

The PD-(L)1 pretreated NSCLC cohort, which enrolled patients who have received prior chemotherapy and anti-PD-(L)1 treatment, provides the most mature dataset from the Company's ongoing biomarker analyses. At the time of data cut-off, there were 6 confirmed partial responses (PRs) among the first 57 patients enrolled, for an 11% objective response rate (ORR) (95% CI: 4-21%) among patients treated with the entinostat-pembrolizumab combination regimen. A total of 4 of the 6 responders were negative for PD-(L)1 expression at study entry. Among the 57 patients enrolled, 22 were refractory to prior PD-(L)1 therapy, and only 4 had a documented prior response to PD-(L)1 therapy. Median duration of prior PD-(L)1 therapy was < 6 months and the median time between last dose of prior PD-(L)1 therapy and first dose with the entinostat-pembrolizumab combination was 65 days. The median duration of response (DOR) to the entinostat-pembrolizumab combination was 4.6 months, with the longest observed response over 14 months. At the time of the data cut-off, 7 patients remain on study.

Blood samples were collected and analyzed for 51 of the 57 NSCLC patients enrolled. By measuring pre-treatment baseline levels of classical peripheral blood monocytes (CD14⁺CD16⁺HLA-DR^{hi}), the Company has been able to identify a subset of patients that appears to exhibit enhanced clinical benefit to the entinostat-pembrolizumab combination regimen. Preliminary results from this assessment indicate that patients characterized by elevated baseline levels of monocytes ("high monocyte" subset, n=14) had a confirmed ORR of 29% (4 PRs/14 patients) and a Progression Free Survival (PFS) of 5.4 months, which compares favorably to the 2.8 month benefit recently demonstrated in NSCLC patients treated with third-line chemotherapy following progression after platinum doublet and PD-(L)1 treatment¹. In contrast, the subgroup of patients characterized by lower baseline levels of monocytes ("low monocyte" subset, n=37) had a confirmed ORR of 5% (2 PRs/37 patients) and a PFS of 2.5 months. The overall patient population (n=57) achieved a PFS of 2.7 months.

Based upon these findings, the Company has identified a potential registration path in patients with NSCLC who have progressed on a PD(L)1 inhibitor. The trial is anticipated to commence by the end of 2018.

"Monocyte levels may reflect the ability of the immune system to respond after elimination of immune suppression," said Dmitry I. Gabrilovich, M.D., Ph.D., Christopher M. Davis Professor and Program Leader, Immunology, Microenvironment and Metastasis Program at The Wistar Institute. "The data from this PD-1 pre-treated population suggest that monocytes are associated with positive clinical outcome from entinostat combined with pembrolizumab, and if confirmed, can potentially be used for patient selection in future studies."

"NSCLC patients whose disease has progressed on PD-(L)1 and chemotherapy are in need of options that offer meaningful clinical benefits. Initial findings from this cohort of NSCLC patients receiving the entinostat-pembrolizumab combination provide encouraging benefit in ORR and PFS," said Leena Gandhi, M.D., Ph.D., Director of Thoracic Medicine Oncology Program at NYU Langone's Perlmutter Cancer Center. "Although more data is needed, promising results for a population of patients with high monocyte counts further highlight that a selection strategy may lead to enhanced benefits for patients."

Melanoma and MSS-CRC Update

Within the anti-PD-1 pretreated melanoma cohort, a total of 6 confirmed PRs (ORR 18%; 95% CI: 6.8-34.5%) and 3 unconfirmed PRs were observed in the 34 evaluable patients at the time of the data cut-off. Among these patients, 16 were PD-1 refractory, and only 2 had a documented response to prior anti-PD-1 therapy. The majority of these evaluable patients, 22 of 34, previously received the anti-CTLA-4 antibody YERVOY® (ipilimumab) in addition to an anti-PD-1 regimen. Two of the 3 patients with unconfirmed responses had progressive disease within 6 weeks of the scan, while the third patient discontinued due to an adverse event. The median duration of prior anti-PD-1 therapy was < 6 months, and the median time between last dose of prior anti-PD-1 therapy and first dose with the entinostat-pembrolizumab combination was 64 days. The median DOR to the entinostat-pembrolizumab combination was 9.1 months. Four of the 34 patients remain on therapy as of the data cut-off date, while 3 of the 34 evaluable patients received therapy for over a year.

Enrollment in this cohort was recently completed (n=55), and further efficacy analyses and biomarker assessments from the recently enrolled patients will be utilized to supplement and strengthen the Company's development strategy for melanoma.

Within the MSS-CRC cohort, 16 patients were initially enrolled, with a median of three lines of prior therapy in the advanced setting. One patient from the initial patient cohort had a confirmed PR and remains on treatment at >6 months. Nine patients experienced stable disease as best response, 2 for at least 4 months. As the Company recently announced, following discussions with investigators and collaborator Merck, the decision was made to expand enrollment of this cohort to include a total of 37 patients in the first stage of the Simon-two stage study. Enrollment is expected to resume into the modified stage 1 cohort by the end of the second quarter, with at least three responses required to advance to the second stage, at which point an additional 47 patients would be enrolled. A decision on whether to continue to the second stage of this cohort is expected in the first half of 2019. As with the other ENCORE 601 cohorts, peripheral blood and pre- and on-treatment biopsies are being evaluated.

The data announced today will be presented in poster presentations at the upcoming ASCO meeting:

Title: Efficacy and safety of entinostat (ENT) and pembrolizumab (PEMBRO) in patients with non-small cell lung cancer (NSCLC) previously treated with anti-PD-(L)1 therapy

First Author: Leena Gandhi, MD, PhD, NYU Perlmutter Cancer Center

Abstract Number: 9036

Poster Session: Lung Cancer—Non-Small Cell Metastatic

Poster Board: 359

Date and Time: Sunday, June 3, 2018, 8:00-11:30 AM CT, Hall A

Title: Efficacy and safety of entinostat (ENT) and pembrolizumab (PEMBRO) in patients with melanoma progressing on or after a PD-1/L1 blocking antibody

First Author: Sanjiv S. Agarwala, MD, St. Luke's Hospital

Abstract Number: 9530

Poster Session: Melanoma/Skin Cancers

Poster Board: 357

Date and Time: Monday, June 4, 2018, 1:15-4:45 PM CT, Hall A

Title: ENCORE 601: A phase 2 study of entinostat in combination with pembrolizumab in patients with microsatellite stable metastatic colorectal cancer

First Author: Nilofer Saba Azad, MD, Sidney Kimmel Cancer Center at Johns Hopkins University

Abstract Number: 3557

Poster Session: Gastrointestinal (Colorectal) Cancer

Poster Board: 50

Date and Time: Sunday, June 3, 2018, 8:00-11:30 AM CT, Hall A

Conference Call and Webcast

In connection with today's announcement, Syndax's management team will host a conference call and live audio webcast at 8:30 a.m. ET today, Thursday, May 17, 2018.

The live audio webcast and accompanying slides may be accessed through the Events & Presentations page in the Investors section of the Company's website at www.syndax.com. Alternatively, the conference call may be accessed as follows:

Conference ID: 5778787

Domestic Dial-in Number: 1-855-251-6663

International Dial-in Number: 281-542-4259

Live webcast: <https://edge.media-server.com/m6/p/j4astqtk>

For those unable to participate in the conference call or webcast, a replay will be available for 30 days on the Investors section of the Company's website, www.syndax.com.

About Syndax Pharmaceuticals, Inc.

Syndax Pharmaceuticals is a clinical stage biopharmaceutical company developing an innovative pipeline of cancer therapies. The Company is developing its lead product candidate, entinostat, a once-weekly, oral, small molecule, class I HDAC inhibitor, in combination with exemestane and several approved PD-1/PD-L1 antagonists. The Company's pipeline also includes SNDX-6352, a monoclonal antibody that blocks the colony stimulating factor 1 (CSF-1) receptor, as well as a portfolio of potent and selective inhibitors targeting the binding interaction of Menin with MLLr. For more information, please visit www.syndax.com or follow the Company on [Twitter](#) and [LinkedIn](#).

Citations

¹ Costantini et. al., ERJ Open Res 2018; 4:00120-2017

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.

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View original content: <http://www.prnewswire.com/news-releases/syndax-announces-updated-results-from-phase-2-encore-601-trial-of-entinostat-in-combination-with-keytruda-pembrolizumab-300650233.html>

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