Syndax Announces U.S. FDA Breakthrough Therapy Designation Granted for Revumenib for the Treatment of Adult and Pediatric Patients with Relapsed or Refractory KMT2A- Rearranged (MLLr) Acute Leukemia

December 5, 2022

-- Revumenib is the first and only investigational treatment for R/R KMT2Ar acute leukemia to receive Breakthrough Therapy Designation --

-- Designation is based on Phase 1 data from the AUGMENT-101 trial that showed a 27% CR/CRh rate in KMT2A patients treated at RP2D --

-- Company remains on track to submit an NDA for revumenib by the end of 2023 with the potential for an expedited approval with a broad indication --

WALTHAM, Mass., Dec. 5, 2022 /PRNewswire/ -- Syndax Pharmaceuticals, Inc. (Nasdaq: SNDX), a clinical-stage biopharmaceutical company developing an innovative pipeline of cancer therapies, today announced that the U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy Designation (BTD) for revumenib for the treatment of adult and pediatric patients with relapsed or refractory (R/R) acute leukemia harboring a KMT2A rearrangement (KMT2Ar). Revumenib is the Company's highly selective, oral menin inhibitor.

"The Breakthrough Therapy Designation underscores revumenib's potential as a first- and best-in-class therapy to meaningfully change the treatment paradigm for patients with R/R KMT2Ar acute leukemia, whether it presents clinically as acute myeloid leukemia (AML) or acute lymphocytic leukemia (ALL), in adults or children," said Michael A. Metzger, Chief Executive Officer. "Revumenib has the potential, if approved, to be the first drug to address the significant unmet need in KMT2Ar leukemia believed to occur in up to 10% of all acute leukemias, including in approximately 80% of infant acute leukemias. Syndax is committed to bringing revumenib to these patients as quickly as possible and we look forward to working collaboratively with the FDA to expedite a potential approval of revumenib."

The BTD is supported by Phase 1 data from the AUGMENT-101 trial. Ten of 37 patients (27%) with age and phenotype agnostic KMT2Ar acute leukemia treated at doses meeting the protocol defined criteria for the recommended Phase 2 dose (RP2D) and evaluable for efficacy as of the March 2022 data cutoff achieved a complete remission as measured by a CR/CRh. Included in this analysis were patients treated in Arm A (226 and 276 mg q12 hours not receiving a strong CYP3A4 inhibitor) and Arm B (113 and 163 mg q12 hours receiving a strong CYP3A4 inhibitor).

As previously announced, additional data from the Phase 1 portion of the AUGMENT-101 trial will be presented during two oral sessions at the American Society of Hematology (ASH) Annual Meeting on December 10, 2022. The abstracts (Abstracts #63 and #376) describe data on the 60 patients with R/R mutant NPM1 (n=14) or KMT2A rearranged (MLLr; n=46) acute leukemia that were evaluable for efficacy as of the March 2022 data cutoff date. Additional analyses from the trial that will be presented at the ASH Annual Meeting indicate a 27% CR/CRh rate at doses meeting the protocol defined criteria for the RP2D in all efficacy evaluable patients (13/48) and in patients with an NPM1 mutation (3/11). There were no discontinuations due to treatment-related adverse events.

The FDA grants BTD to expedite the development and regulatory review of drugs that are intended for serious or life-threatening conditions. The designation is based on preliminary clinical evidence indicating that a drug may demonstrate substantial improvement on at least one clinically significant endpoint over available therapy. BTD affords all of the benefits of the fast track program, eligibility for rolling review and potentially priority review, and additional engagement to facilitate an expedited development plan and regulatory review.

About Revumenib

Revumenib is a potent, selective, small molecule inhibitor of the menin-MLL binding interaction that is being developed for the treatment of KMT2A rearranged, also known as mixed lineage leukemia rearranged or MLLr, acute leukemias including acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML), and NPM1 mutant AML. Revumenib is currently being evaluated in several clinical trials, including the Company's pivotal AUGMENT-101 Phase 1/2 open-label clinical trial for the treatment of relapsed/refractory (R/R) acute leukemias. Robust clinical activity with durable responses have been reported in the Phase 1 portion of AUGMENT-101. Revumenib was granted Orphan Drug Designation by the U.S. Food and Drug Administration (FDA) and European Commission for the treatment of patients with AML, and Fast Track designation by the FDA for the treatment of adult and pediatric patients with R/R acute leukemias harboring a KMT2A rearrangement or NPM1 mutation.

About KMT2A (MLL) Rearranged Acute Leukemia

Rearrangements of the KMT2A (mixed lineage leukemia or MLL) gene give rise to KMT2Ar acute leukemia known to have a poor prognosis, with less than 25% of adult patients surviving past five years. KMT2A genes produce fusion proteins that require interaction with the protein called menin to drive leukemic cancer growth. Disruption of the menin-KMT2Ar interaction has been shown to halt the growth of KMT2Ar leukemic cells.

KMT2Ar acute leukemia can phenotypically appear as AML, ALL, or mixed phenotype acute leukemia (MPAL) and is routinely diagnosed through currently available cytogenetic or molecular diagnostic techniques. The median overall survival (OS) after standard of care first-line treatment, including intensive chemotherapy and transplant, is less than 1 year and the majority of patients suffer relapse within 5 years. Most R/R patients treated with second-line therapy relapse within the first year. With third line treatment or beyond, only a small percentage of patients achieve complete remission (CR), and the median OS is less than 3 months.

About AUGMENT-101

AUGMENT-101 is a Phase 1/2 open-label trial designed to evaluate the safety, tolerability, pharmacokinetics, and efficacy of orally administered revumenib. The Phase 1 dose escalation portion of AUGMENT-101 was separated into two cohorts based on concomitant treatment with a strong CYP3A4 inhibitor. Arm A enrolled patients not receiving a strong CYP3A4 inhibitor, while Arm B enrolled patients receiving a strong CYP3A4 inhibitor. The Phase 2 pivotal portion of AUGMENT-101 is currently underway. Patients will be enrolled across each of the following trial populations: patients with NPM1 mutant AML, patients with KMT2Ar (MLLr) AML, and patients with KMT2Ar (MLLr) ALL. Discussions with the FDA have confirmed that

AUGMENT-101 may potentially serve as the basis for regulatory filings in each patient population. The primary endpoint for each of the trials will be efficacy as measured by complete remission rate (CR + CRh), with key secondary endpoints including duration of response (DOR) and overall survival (OS).

About Syndax Pharmaceuticals, Inc.

Syndax Pharmaceuticals is a clinical stage biopharmaceutical company developing an innovative pipeline of cancer therapies. Highlights of the Company's pipeline include revumenib (SNDX-5613), a highly selective inhibitor of the menin–MLL binding interaction, and axatilimab, a monoclonal antibody that blocks the colony stimulating factor 1 (CSF-1) receptor, both currently in pivotal trials. For more information, please visit www.syndax.com or follow the Company on Twitter and LinkedIn.

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, the reporting of clinical data for Syndax's product candidates, the progress of regulatory submissions and approvals, including the impact of Breakthrough Therapy Designation on the timeline for approval of revumenib, and the potential use of Syndax's product candidates to treat various cancer indications and fibrotic diseases. Many factors may cause differences between current expectations and actual results, including: unexpected safety or efficacy data observed during preclinical or clinical trials; clinical trial site activation or enrollment rates that are lower than expected; changes in expected or existing competition; changes in the regulatory environment; the impact of macroeconomic conditions (such as COVID-19 pandemic, the Russia-Ukraine war, inflation, among others) on Syndax's business and that of the third parties on which Syndax depends, including delaying or otherwise disrupting Syndax's clinical trials and preclinical studies, manufacturing and supply chain, or impairing employee productivity; 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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