Syndax Pharmaceuticals Announces Two Publications in Nature of Data from the Phase 1 Portion of AUGMENT-101 in Acute Leukemia Patients

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WALTHAM, Mass., March 15, 2023 /PRNewswire/ -- Syndax Pharmaceuticals, Inc. (Nasdaq: SNDX) today announced that data from the Phase 1 portion of the ongoing Phase 1/2 AUGMENT-101 trial of revumenib in patients with nucleophosmin mutant (mNPM1) and KMT2A-rearranged (KMT2Ar) relapsed/refractory (R/R) acute leukemia and an analysis describing MEN1 mutations observed in the study have been published in the journal *Nature*. Revumenib is the Company's highly selective, oral menin inhibitor.

The Phase 1 publication entitled "*The menin inhibitor revumenib in KMT2A-rearranged or NPM1-mutant leukaemia*" includes positive data from 68 patients with R/R acute leukemia evaluable for safety, 60 patients of whom had mNPM1 or KMT2Ar acute leukemia and were evaluable for efficacy. In these heavily pretreated patients with a median of four prior therapies, 30% (18/60) experienced a CR/CRh with a median duration of CR/CRh response of 9.1 months. Revumenib was well-tolerated, and there were no discontinuations due to treatment-related adverse events. The Phase 1 data were recently featured in two oral presentations at the 64th American Society of Hematology Annual Meeting.

"We are excited to have our Phase 1 AUGMENT-101 data published in such a prominent peer-reviewed journal. As we continue to deepen our understanding of the tumor biology driven by the menin-KMT2A interaction, we gain more evidence to support the potential of revumenib as a best-in-class treatment for both mNPM1 and KMT2Ar acute leukemias," said Michael A. Metzger, Chief Executive Officer. "With the expectation of topline data from the pivotal AUGMENT-101 trial beginning in the third quarter of 2023, followed by a potential New Drug Application filing by the end of 2023, revumenib could become the first menin inhibitor approved for patient use."

A separate companion article published in *Nature* entitled "*MEN1 mutations mediate clinical resistance to menin inhibition*" describes somatic mutations in MEN1 that confer resistance to menin inhibitor treatment and further confirm the dependency of mNPM1 and KMT2Ar acute leukemias on the menin-KMT2A interaction. This represents the first report that menin inhibitors exert sufficient selective pressure to drive evolution of escape mutants that confer resistance to all first generation menin inhibitors and impact both mNPM1 and KMT2Ar acute leukemia. These data were highlighted in an oral presentation at the 64th American Society of Hematology Annual Meeting.

"The robust clinical dataset from a heavily pretreated relapsed/refractory patient population demonstrates that revumenib monotherapy was associated with encouraging clinical benefit, including deep molecular remissions and durable responses, with minimal toxicities," said Ghayas C. Issa, M.D., Assistant Professor, Department of Leukemia, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center and a corresponding author of the Phase 1 publication. "The identified resistance, a class effect among first-generation menin inhibitors, further validates the menin-KMT2A interaction as the key driver for both mNPM1 and KMT2Ar leukemias. Future and ongoing trials may indicate whether treating patients in earlier settings and in combination would provide higher response rates in mNPM1 or KMT2Ar acute leukemia patients who are less likely to have developed functional mutations."

Overview of Phase 1 Data
The Phase 1 publication in *Nature* includes data from 68 patients evaluable for safety, 60 patients of whom were evaluable for efficacy, as of a March 2022 data cutoff. Patients were heavily pretreated with a median of four prior therapies, and 46% (31/68) of the patients had at least one prior stem cell transplant. Within the efficacy evaluable population, the overall response rate was 53% (32/60) with a CR/CRh rate of 30% (18/60), and 78% (14/18) of patients with CR/CRh attaining measurable residual disease (MRD) negativity. The median time to CR/CRh response in the trial was 1.9 months, and the median duration of CR/CRh response was 9.1 months in the efficacy evaluable population as of data cutoff. A total of 38% (12/32) of responders proceeded to transplant, with nine in remission at the time of the data cutoff, seven of whom have been in remission for greater than six months and four who have been in remission for greater than a year. Eleven (92%) patients who underwent a transplant were MRD negative prior to transplant.

Revumenib was well-tolerated, and no new safety signals were identified in the trial, including in patients who proceeded to stem cell transplant. There were no discontinuations due to treatment-related adverse events. The only dose limiting toxicity was asymptomatic Grade 3 QT prolongation, observed in 10% of patients treated at or below the RP2D and 13% of patients treated at all doses tested. No ventricular arrythmias or other clinical sequelae related to QTc prolongation were reported. Differentiation syndrome occurred in 16% of patients, all which were Grade 2, and patients responded to standard management of steroids with or without hydroxyurea.

About Revumenib
Revumenib is a potent, selective, small molecule inhibitor of the menin-KMT2A 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. Revumenib was also granted Breakthrough Therapy Designation by the FDA for the treatment of adult and pediatric patients with R/R acute leukemia harboring a KMT2A rearrangement.

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 included 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 the following trial populations: patients with NPM1-mutant AML, patients with KMT2Ar AML, and patients with KMT2Ar ALL, each of which may serve as the basis for regulatory filings. Following the receipt of Breakthrough Therapy designation from the FDA for revumenib for the treatment of R/R acute leukemia harboring a KMT2A rearrangement, regardless of age or tumor type, and based on discussions with the FDA, the Company will pool data from the AUGMENT-101 cohorts enrolling R/R KMT2Ar AML and R/R KMT2Ar ALL to file a single NDA for the treatment of adult and pediatric KMT2Ar acute leukemia. The primary

endpoint for each of the trials is efficacy as measured by complete remission rate (CR + CRh), with key secondary endpoints including duration of response (DOR) and overall survival (OS).

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 one year and the majority of patients suffer relapse within five 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 three months. There are currently no approved therapies indicated for KMT2A- rearranged acute leukemia.

About NPM1-Mutant Acute Myeloid Leukemia
NPM1-mutant acute myeloid leukemia (AML), which is distinguished by mutations in the NPM1 gene that drive the leukemic phenotype, is the most common type of cytogenetically normal adult AML and represents approximately 30% of all adult AML cases. This subtype of AML has a five-year overall survival rate of approximately 50%. Similar to KMT2A- rearranged acute leukemia, NPM1-mutant AML is highly dependent on the expression of specific developmental genes shown to be negatively impacted by inhibitors of the menin-KMT2A interaction. NPM1-mutant AML is routinely diagnosed through currently available screening techniques. There are currently no approved therapies indicated for NPM1-mutant AML.

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, a highly selective inhibitor of the menin–KMT2A binding interaction, and axatilimab, a monoclonal antibody that blocks the colony stimulating factor 1 (CSF-1) receptor, both currently in pivotal clinical 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 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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