Syndax Pharmaceuticals Announces Preclinical Profile and Initial Phase 1 Data Demonstrating Clinical Activity of Menin Inhibitor SNDX-5613 in Adults with Relapsed/Refractory Acute Leukemias

April 27, 2020

- Preliminary Phase 1 results represent first clinical evidence that inhibition of the menin-MLL1 interaction can induce response in patients with MLL-r acute leukemias -

- Data featured in New Drugs on the Horizon oral session at the 2020 AACR Virtual Annual Meeting I -

- U.S. FDA grants orphan drug designation to SNDX-5613 for the treatment of adult and pediatric acute myeloid leukemia -

WALTHAM, Mass., April 27, 2020 /PRNewswire/ -- Syndax Pharmaceuticals, Inc. ("Syndax," the "Company" or "we") (Nasdaq: SNDX), a clinical stage biopharmaceutical company developing an innovative pipeline of cancer therapies, today presents preclinical and initial clinical data for SNDX-5613, the Company's potent, highly selective oral menin inhibitor. The oral presentation will be featured during the New Drugs on the Horizon session at the 2020 American Association for Cancer Research (AACR) Virtual Annual Meeting I. The New Drugs on the Horizon session will take place today at 4:50 p.m. ET and features discussions of innovative small molecules and biologics that have recently entered Phase 1 clinical trials.

"Within months of initiating the Phase 1/2 AUGMENT-101 trial, we are excited to present to the cancer research community the first clinical evidence that disrupting the interaction between menin and MLL1 with our potent and selective inhibitor, SNDX-5613, can induce response in patients with genetically-defined acute leukemias," said Briggs W. Morrison, M.D., Chief Executive Officer of Syndax. "Notably, clinical activity was achieved rapidly after a single, 28-day cycle, a highly encouraging sign in this population of patients who face a particularly poor prognosis with few effective treatment options. We look forward to presenting additional findings from this trial in the fourth quarter."

The Company also announced today that SNDX-5613 was recently granted Orphan Drug Designation for the treatment of adult and pediatric acute myeloid leukemia (AML) by the U.S. Food and Drug Administration (FDA).

Preliminary AUGMENT-101 Data

As of the April 17th data cutoff date, a total of six patients have been treated in the Phase 1 portion of the ongoing open-label AUGMENT-101 trial at increasing dose levels of SNDX-5613. Responses were observed in two of three patients harboring an MLL rearrangement. This included one patient, whose drug exposure was consistent with that needed for activity in preclinical models, who had a complete response with incomplete blood count recovery (CRi) after 28 days of therapy and subsequently improved to a complete response (CR). The second patient achieved a partial response with incomplete blood count recovery (PRi) after 28 days of therapy. Both patients continue to receive SNDX-5613. A third patient harboring an MLL rearrangement did not achieve drug exposure levels consistent with that needed for activity in preclinical models and was removed from the trial due to progressive disease. Treatment with SNDX-5613 has been tolerated well, with no dose limiting toxicities reported. One patient experienced a Grade 2 QTc prolongation but remains on treatment. Additional details regarding all six patients are available in the AACR presentation.

"Three decades of scientific research exploring the menin-MLL-r interaction and its importance in this subset of leukemias have helped establish our confidence in the therapeutic potential of SNDX-5613 for leukemia patients harboring MLL-r and NPM1 mutations," said Jerry McGeehan, Ph.D., Vice President, Menin Program at Syndax Pharmaceuticals. "Following the recently published preclinical studies in *Cancer Cell* and *Science* magazine highlighting the activity of menin inhibition in genetically-defined leukemias, we are thrilled to demonstrate in the clinical setting that SNDX-5613 could serve as a targeted agent with the potential to deliver durable benefit to a severely underserved patient population."

The Company's presentation also highlighted preclinical data supporting the potential of single-agent menin-MLL inhibition to serve as an effective intervention for both NPM1 mutant AML and MLL-r acute leukemias.

The AUGMENT-101 trial is a Phase 1/2 open-label trial designed to evaluate the safety, tolerability, pharmacokinetics and efficacy of orally administered SNDX-5613. The Phase 1 dose escalation portion of AUGMENT-101 was recently separated into two cohorts based on concomitant treatment with a strong CYP3A4 inhibitor. Arm A will enroll patients not receiving a strong CYP3A4 inhibitor, while Arm B will enroll patients receiving a strong CYP3A4 inhibitor. The Phase 1 dose escalation portion of AUGMENT-101 is currently enrolling adults with R/R acute leukemias including MLL-r and nucleophosmin (NPM1) mutant acute leukemias and is expected to establish a recommended Phase 2 dose for both cohorts by the fourth quarter of 2020. The Phase 2 portion will evaluate efficacy, as defined by CR rate (per International Working Group response criteria), across three expansion cohorts: MLL-r acute lymphoblastic leukemia (ALL), MLL-r AML and NPM1 mutant AML. MLL rearrangements are seen in 5-10% of AML and ALL, while NPM1 mutations are seen in 30% of adult AML cases. The Company expects to present additional results from AUGMENT-101 at a medical conference in the fourth quarter of 2020.

Additional AACR Presentations

In addition to the SNDX-5613 presentation, data from the Phase 1 trials of the Company's anti-CSF-1R monoclonal antibody, axatilimab, both as a monotherapy and in combination with IMFINZI® (durvalumab) in patients with locally-advanced or metastatic solid tumors, were summarized in two oral presentations. These data indicate that axatilimab is tolerated well in solid tumor patients, generated a recommended Phase 2 dose for axatilimab for the treatment of patients with solid tumors, and provided evidence of its ability to deplete circulating pro-inflammatory monocytes.

A copy of all AACR presentations will be available via Syndax's website at http://www.syndax.com/science/publications/.

About SNDX-5613

SNDX-5613 is a potent, selective, small molecule inhibitor of the menin-MLL binding interaction that is being developed for the treatment of MLL-rearranged (MLL-r) acute leukemias, including acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML) and NPM1 mutant AML.

In preclinical models of MLL-r acute leukemias, SNDX-5613 demonstrated robust, dose-dependent inhibition of tumor growth, resulting in a marked survival benefit. Menin-MLL interaction inhibitors have also demonstrated robust treatment benefit in multiple preclinical models of NPM1 mutant AML, which represents the most frequent genetic abnormality in adult AML. SNDX-5613 is currently being evaluated in the Company's AUGMENT-101 Phase 1/2 open-label clinical trial for the treatment of relapsed/refractory (R/R) acute leukemias.

About Mixed Lineage Leukemia Rearranged (MLL-r)

Rearrangements of the MLL gene give rise to MLL-r acute leukemias, known to have a poor prognosis, with less than 55% of patients surviving past 5 years. MLL rearrangements produce fusion proteins that require interaction with the protein called menin to drive leukemic cancer growth. Disruption of the menin-MLL-r interaction has been shown to halt the growth of MLL-r leukemic cells. MLL-r leukemias, which are routinely diagnosed through currently available cytogenetic or molecular diagnostic techniques, occur in approximately 80% of infant acute leukemias and up to 10% of all acute leukemias. There are currently no approved therapies indicated for MLL-r leukemias.

About NPM1 Mutant Acute Myeloid Leukemia

NPM1 mutant AML, which is distinguished by point 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 5-year overall survival rate of approximately 50%. Similar to MLL-r leukemias, NPM1 mutant AML is highly dependent on the expression of specific developmental genes, shown to be negatively impacted by inhibitors of the menin-MLL interaction. NPM1 mutant AML is routinely diagnosed through currently available screening techniques. There are currently no approved therapies indicated for NPM1 mutant AML.

About Orphan Drug Designation

The Orphan Drug Designation program provides orphan status to drugs and biologics that are intended for the safe and effective treatment, diagnosis, or prevention of rare diseases that affect fewer than 200,000 people in the U.S. Among the benefits of orphan designation in the U.S. are seven years of market exclusivity following FDA approval, waiver or partial payment of application fees, and tax credits for clinical testing expenses conducted after orphan designation is received.

About Syndax Pharmaceuticals, Inc.

Syndax Pharmaceuticals is a clinical stage biopharmaceutical company developing an innovative pipeline of cancer therapies. The Company's lead product candidate, entinostat, a once-weekly, oral, small molecule, class I HDAC inhibitor, is being tested in a Phase 3 combination trial with exemestane for treatment of advanced HR+, HER2- breast cancer and has been evaluated in combination with several approved PD-1/PD-(L)1 antagonists. The Company's pipeline also includes axatilimab, a monoclonal antibody that blocks the colony stimulating factor 1 (CSF-1) receptor, and SNDX-5613, a highly selective inhibitor of the menin–MLL binding interaction. For more information, please visit www.syndax.com or follow the Company on Twitter and LinkedIn.

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 trials, 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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