Science Magazine Publishes Results from Preclinical Study on the Activity of Menin-MLL Inhibition for the Treatment of NPM1 Acute Myeloid Leukemia

January 30, 2020

- Results support ongoing Phase 1/2 AUGMENT-101 trial of Syndax Pharmaceuticals' lead Menin-MLL inhibitor, SNDX-5613, for the treatment of adults with relapsed/refractory acute leukemias, including NPM1 mutant AML -

WALTHAM, Mass., Jan. 30, 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 announced that *Science* magazine has published a preclinical report supporting the potential role of MLL1-Menin inhibition in the management of nucleophosmin (NPM1) mutant acute myeloid leukemia (AML). The article, "Therapeutic targeting of preleukemia cells in a mouse model of NPM1 mutant acute myeloid leukemia," will be published in the journal's January 31, 2020 issue and is currently available online.

This study examined the activity of VTP-50469, an orally-available inhibitor of MLL1-Menin interaction and close analog of the Company's lead Menin inhibitor, SNDX-5613, for the treatment of established NPM1 AML and the possible prevention of the disease in high-risk populations. Using preclinical models of NPM1 AML, the authors established that the presence of an NPM1 mutation is a clear indicator of pre-leukemic activity and represents a critical step in the development of AML. VTP-50469 was shown to eradicate NPM1 mutant cells at various stages of disease development, suggesting that Menin-MLL inhibition could potentially serve either as a targeted preventive therapy or as a treatment of established disease.

"These unprecedented findings highlight the potential for single agent Menin-MLL inhibition to rapidly eradicate fully developed NPM1 mutant leukemia, even in the case of aggressive relapsed AML," said Scott A. Armstrong, M.D., Ph.D., President, Dana-Farber/Boston Children's Cancer and Blood Disorders Center, and Chairman, Department of Pediatric Oncology, Dana-Farber Cancer Institute, and senior author of the study. "In addition, these results provide support for a Menin-MLL inhibitor to serve as a novel strategy to prevent AML development in high-risk patient populations, as NPM1 mutations are acquired in pre-leukemic clones."

"NPM1 mutant AML represents the most common type of cytogenetically normal AML," said Briggs W. Morrison, M.D., Chief Executive Officer of Syndax. "On the heels of our recent *Cancer Cell* publication, these findings add to the growing body of compelling preclinical data supporting the potential for SNDX-5613 to serve as an effective intervention for both NPM1 mutant AML and MLL-r acute leukemias. We are committed to providing patients with more targeted therapeutic options and are hopeful that these findings will translate into the clinic in our ongoing Phase 1/2 AUGMENT-101 trial."

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); VTP-50469 is a close analog of SNDX-5613. MLL rearrangements occur in approximately 80% of acute leukemia cases in infants and up to 10% of all leukemias. 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 AUGMENT-101

AUGMENT-101 is a Phase 1/2 open-label trial designed to evaluate the efficacy, safety, tolerability and pharmacokinetics of orally administered SNDX-5613. The Phase 1 dose escalation portion of AUGMENT-101 will enroll adults with R/R acute leukemias and establish a recommended Phase 2 dose. The Phase 2 portion will evaluate efficacy, as defined by Complete Response rate (per International Working Group response criteria), across three expansion cohorts: MLL-r ALL, MLL-r AML and NPM1 mutant AML. The Company expects to report initial clinical data from the trial in 2020. Additional information about the AUGMENT-101 trial is available via Clinicaltrials.gov (NCT 04065399).

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 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 SNDX-6352, 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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