Syndax Pharmaceuticals Announces Additional Positive Data Demonstrating Continued Robust Clinical Activity with Durable Responses in Phase 1 Portion of AUGMENT-101 Trial of SNDX-5613

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- 55% overall response rate and 24% CR/CRh rate in relapsed/refractory acute leukemia patients with NPM1 or MLLr mutations; no discontinuations due to treatment-related adverse events -

- CR/CRh rates of 23% and 24% in mNPM1 and MLLr patients, respectively -

- CR/CRh responses were durable; median duration of response was not reached; 50% persisted longer than 6 months -

WALTHAM, Mass., Dec. 13, 2021 /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 positive data from the Phase 1 dose escalation portion of the AUGMENT-101 trial of SNDX-5613 in patients with mutant nucleophosmin (mNPM1) or mixed lineage leukemia rearranged (MLLr) relapsed/refractory (R/R) acute leukemias. SNDX-5613 is the Company's highly selective oral menin inhibitor. The data are being featured during an oral session at the 63rd American Society of Hematology (ASH) Annual Meeting on Monday, December 13, 2021 at 3:15 p.m. ET.

"Patients with relapsed or refractory leukemia harboring NPM1 mutations or MLL-rearrangements face a particularly poor prognosis," said Eytan M. Stein, M.D., Assistant Attending Physician and Director, Program for Drug Development in Leukemia, Department of Medicine at Memorial Sloan Kettering Cancer Center, and the trial's principal investigator. "Data being reported today show highly encouraging clinical activity and favorable tolerability across a heavily pretreated population. In addition to very high MRD negative rates in those patients achieving complete response (CR) or CR with partial hematologic recovery (CRh), we are also seeing response durations greater than six months."

"The updated data presented today at ASH from our ongoing AUGMENT-101 trial strongly support the potential of SNDX-5613 to serve as a best-in-class treatment option for patients with NPM1 or MLLr leukemia, which together represents approximately 40% of all acute leukemias," said Briggs W. Morrison, M.D., Chief Executive Officer of Syndax. "We are also very pleased that discussions with the U.S. Food and Drug Administration (FDA) have confirmed that the ongoing Phase 2 AUGMENT-101 trial may potentially serve as the basis for regulatory filings in each of its three indication-specific cohorts of NPM1 mutant acute myeloid leukemia (AML), MLLr AML, and MLLr acute lymphoblastic leukemia (ALL), and that patients will be able to restart treatment with SNDX-5613 following a stem cell transplant."

Dr. Morrison continued, "We also remain focused on executing on our strategy to expand into earlier lines of therapy and pediatric populations, and we look forward to initiating the BEAT AML trial in frontline MLLr and mNPM1 AML in combination with venetoclax and azacitidine, the INTERCEPT trial in AML patients with MRD positive disease, and the AUGMENT-102 trial in combination with chemotherapy in adult and pediatric relapsed/refractory MLLr and mNPM1 acute leukemia patients."

As of an October 18, 2021 data cutoff date, a total of 59 patients with a median of four prior therapies, including 42% who received a prior stem cell transplant and 59% who received prior venetoclax, were dosed in the Phase 1 portion of the trial. Across evaluable patients with mNPM1 (n=13) or MLLr (n=38) acute leukemia who received at least one dose of SNDX-5613, the overall response rate[1] (ORR) was 55%, with a CR/CRh rate of 24% and nine patients proceeding to stem cell transplant (two patients achieving a CR with incomplete platelet recovery [CRp] with no evidence of minimal residual disease [MRD], and seven patients who achieved MRD- CR or CRh). The ORR in evaluable patients harboring an NPM1 mutation was 38% (5/13), with a CR/CRh rate of 23% (3/13). The ORR in evaluable patients harboring an MLL-rearrangement was 61% (23/38), with a CR/CRh rate of 24% (9/38).

The overall MRD negative rate was 31% (16/51). Among those patients who achieved CR/CRh, 92% (11/12) were MRD negative, including 100% (3/3) of NPM1 patients and 89% (8/9) of MLLr patients. Median time to response for patients achieving a CR/CRh was two months. Median duration of response (DOR) was not reached, inclusive of patients who received stem cell transplant, and 6/12 patients who achieved CR/CRh had a duration of response greater than six months.

SNDX-5613 was well-tolerated, with no discontinuations due to treatment-related adverse events observed in heavily pretreated patients. The only dose limiting toxicity observed was Grade 3 QT prolongation, which occurred in 7% (3/43) of patients treated at the four doses that met the study's pre-defined recommended Phase 2 dose criteria. Differentiation syndrome was reported in 14% of patients (8/59) with all cases being Grade 1 or 2 and readily managed with standard therapies.

As data from the Phase 1 portion of the trial have continued to mature, the results have demonstrated consistent and compelling anti-leukemic activity with favorable tolerability in patients with both R/R MLLr and NPM1 acute leukemias. The following table summarizes select efficacy and safety data that has been presented by the Company throughout 2021.

Best Response in Response Evaluable Patients	**April '21 n = 31 (%)**	**May '21 n = 31 (%)**	**Dec '21 n = 51 (%)**
Overall Response Rate* (ORR)	**15/31 (48%)**	**15/31 (48%)**	**28/51 (55%)**
CR/CRh	5 (16%)	7 (23%)	12 (24%)
CRp	5 (16%)	4 (13%)	7 (14%)
CRi/MLFS	5 (16%)	4 (13%)	9 (18%)
Received HSCT	4	4	9
MLLr ORR	13/24 (54%)	13/24 (54%)	23/38 (61%)
mNPM1 ORR	2/7 (29%)	2/7 (29%)	5/13 (38%)
≥Gr3 QTc prolonged (all doses)	14%	14%	12%
≥Gr3 QTc prolonged (RP2D doses)	9%	9%	7%

* Overall Response Rate = CR + CRh + CRp + CRi + MLFS

The Phase 2 portion of AUGMENT-101, which will assess 163 mg every 12 hours of SNDX-5613 in patients receiving concomitant strong CYP3A4 inhibitor treatment, is currently underway. A total of 64 adult and up to ten pediatric patients will be enrolled across each of the following three distinct trial populations: patients with NPM1 mutant AML, patients with MLLr AML, and patients with MLLr ALL. Discussions with the FDA have confirmed that AUGMENT-101 may potentially serve as the basis for regulatory filings in each of the three distinct trials. The primary endpoint for each of the three trials will be efficacy as measured by complete remission rate (CR + CRh), with key secondary endpoints including DOR and overall survival.

A copy of today's presentation will be available in the Publications and Meeting Presentations section of Syndax's website.

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 mixed lineage leukemia rearranged (MLLr) acute leukemias including acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML), and NPM1 mutant AML. In preclinical models of MLLr 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. SNDX-5613 was granted Orphan Drug Designation by the U.S. Food and Drug Administration for the treatment of patients with AML, and Fast Track designation for the treatment of adult and pediatric patients with relapsed or refractory acute leukemias harboring a mixed lineage leukemia rearranged MLLr or NPM1 mutation.

About Mixed Lineage Leukemia Rearranged Acute Leukemias

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

About NPM1 Mutant Acute Myeloid Leukemia

NPM1 mutant acute myeloid leukemia (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 five-year overall survival rate of approximately 50%. Similar to mixed lineage leukemia rearranged (MLLr) 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 pipeline includes SNDX-5613, a highly selective inhibitor of the Menin–MLL binding interaction, axatilimab, a monoclonal antibody that blocks the colony stimulating factor 1 (CSF-1) receptor, and entinostat, a class I HDAC inhibitor. For more information, please visit www.syndax.com or follow the Company on Twitter and LinkedIn.

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, the reporting of clinical data for Syndax's product candidates, and the potential use of our 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 COVID-19 pandemic may disrupt our business and that of the third parties on which we depend, including delaying or otherwise disrupting our 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 in our Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on September 15, 2021, as well as in other filings we may make with the SEC in the future. 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.

Reference

1. ORR = CR + CRh + CRp + MLFS

Disclosure: Dr. Stein has provided consulting services for Syndax

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