Syndax Announces Positive Updated Data from Phase 1 Portion of AUGMENT-101 Trial of Revumenib in Patients with Acute Leukemias During Oral Presentations at 64th ASH Annual Meeting

December 10, 2022

- 30% CR/CRh rate in efficacy evaluable population; 27% CR/CRh rate observed in both mNPM1 and KMT2Ar (MLLr) R/R acute leukemia patients treated at RP2D -

- 9 of 12 patients who underwent stem cell transplant after achieving a response with revumenib remained in remission, with four continuing beyond one year -

- Company to host conference call and webcast on Sunday, December 11, 2022 at 8:00 a.m. CT/ 9:00 a.m. ET -

WALTHAM, Mass., Dec. 10, 2022 /PRNewswire/ -- Syndax Pharmaceuticals, Inc. (Nasdaq: SNDX), a clinical-stage biopharmaceutical company developing an innovative pipeline of cancer therapies, today presented updated positive 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 (KMT2r) relapsed/refractory (R/R) acute myeloid or acute lymphoid leukemias (ALL or AML). Revumenib is the Company's highly selective, oral menin inhibitor. The data were featured during two oral sessions today at the 64th American Society of Hematology (ASH) Annual Meeting.

"Both AUGMENT-101 data presentations featured today at the ASH Annual Meeting highlight revumenib's compelling clinical profile and continue to support the potential for revumenib to be a first-in-class and best-in-class therapy for both KMT2Ar and NPM1 acute leukemias," said Michael A. Metzger, Chief Executive Officer. "We previously announced that revumenib received Breakthrough Therapy Designation for the treatment of adult and pediatric patients with R/R acute leukemia (AML or ALL) harboring KMT2A rearrangements, further emphasizing the compelling data that we have generated in the Phase 1 portion of the trial that included 46 R/R KMT2Ar acute leukemia patients as well as the unmet need that exists in this population. We remain on track to report top-line data from at least one of the cohorts from the pivotal Phase 2 portion of the trial beginning in the third quarter of 2023, followed by a potential New Drug Application filing by the end of 2023."

"Patients with genetically-defined acute leukemias, including those harboring NPM1 mutations and KMT2A-rearrangements, have a limited number of effective treatment options and face a particularly poor prognosis," said Ghayas C. Issa, M.D., Assistant Professor, Department of Leukemia, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center. "The deep, durable responses and manageable safety profile observed continue to support the potential for revumenib to serve as a meaningful new addition to the treatment armamentarium for this patient population. I look forward to contributing to the continued advancement of this promising therapeutic option."

The oral presentation titled "The Menin Inhibitor Revumenib (SNDX-5613) Leads to Durable Responses in Patients with KMT2A-Rearranged or NPM1 Mutant AML: Updated Results of a Phase 1 Study" featured updated results from the Phase 1 portion of the AUGMENT-101 trial. As of the March 2022 data cutoff date, 60 patients with R/R mutant NPM1 or KMT2Ar acute leukemia were efficacy evaluable. In the efficacy evaluable population, the ORR was 53% (32/60) with a CR/CRh rate of 30% (18/60), and 78% (14/18) of patients with CR/CRh attaining minimal residual disease (MRD) negativity. Additional analyses from the trial indicate that at doses which met the protocol defined criteria for a recommended Phase 2 dose (RP2D), the CR/CRh rate was 27% in both the KMT2Ar (10/37) and the mutant NPM1 (3/11) patient populations. A total of 38% (12/32) of responders proceeded to transplant. The median time to 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.

Additional results included:

Best Response	Efficacy Population (N=60)	Efficacy Population Doses Meeting Criteria for RP2D (n=48)
Response		
Overall response rate[1], n, (%)	32 (53 %)	25 (52 %)
CR/CRh	18 (30 %)	13 (27 %)
CR	12 (20 %)	8 (17 %)
CRh	6 (10 %)	5 (10 %)
CRp	5 (8 %)	5 (10 %)
MLFS	9 (15 %)	7 (15 %)
MRD^{neg} rate[2]	18/32 (56%)	14/25 (56%)
within CR/CRh MRD^{neg}, n, (%)	14/18 (78%)	10/13 (77%)
within CR/CRh/CRp MRD^{neg}, n, (%)	18/23 (78%)	14/18 (78%)
KMT2Ar (MLLr)		
Overall response rate[1], n, (%)	27/46 (59%)	20/37 (54%)
CR/CRh	15/46 (33%)	10/37 (27%)
mNPM1		
Overall response rate[1], n, (%)	5/14 (36%)	5/11 (46%)
CR/CRh	3/14 (21%)	3/11 (27%)

1. Overall Response Rate = CR+CRh+CRp+MLFS; 2. MRD status assessed locally by PCR or MCF

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 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, and all cases of differentiation syndrome were Grade 2, and responded to standard management of steroids with or without hydroxyurea.

The oral presentation titled "Outcomes After Transplant in Relapsed/Refractory KMT2Ar (MLLr) and mNPM1 (NPM1c) Leukemia Patients Achieving Remissions After Menin Inhibition: Revumenib (SNDX-5613) Ph1 Experience" describes outcomes after transplant in patients achieving remissions in the Phase 1 portion of the AUGMENT-101 trial. Across evaluable patients with mNPM1 (n=14) or MLLr (n=46) acute leukemia who received revumenib, 12 (20%) patients proceeded to stem cell transplant, 11 (92%) of whom were MRD negative prior to transplant. Nine of the 12 patients (75%) who received a stem cell transplant remained in remission as of the data cutoff date, with a median follow-up of 12.3 months, and four patients experienced remission for longer than one year without additional maintenance therapy.

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

Conference Call and Webcast

The Company will host a conference call and webcast to discuss the ASH data update tomorrow, Sunday, December 11, 2022 at 8:00 a.m. CT/ 9:00 a.m. ET. Joining the call will be members of the Syndax management team as well as two of the Primary Investigators on the AUGMENT-101 trial [Eytan M. Stein, M.D., Assistant Attending Physician and Director, Program for Drug Development in Leukemia, Department of Medicine at Memorial Sloan Kettering Cancer and Ghayas C. Issa, M.D., Assistant Professor, Department of Leukemia, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center].

The live audio webcast and accompanying slides may be accessed through the Events & Presentations page in the Investors section of the Company's website. Alternatively, the conference call may be accessed through the following:

Conference ID: SYNDAX12
Domestic Dial-in Number: 800-225-9448
International Dial-in Number: 203-518-9708
Live webcast: https://www.veracast.com/webcasts/OpenEx/General/p08Np3.cfm

For those unable to participate in the conference call or webcast, a replay will be available on the Investors section of the Company's website at www.syndax.com approximately 24 hours after the conference call and will be available for a limited time.

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. 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 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 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 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 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. 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 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.

Syndax Contact

Sharon Klahre
Syndax Pharmaceuticals, Inc.
sklahre@syndax.com
Tel 781.684.9827

SNDX-G

View original content:https://www.prnewswire.com/news-releases/syndax-announces-positive-updated-data-from-phase-1-portion-of-augment-101-trial-of-revumenib-in-patients-with-acute-leukemias-during-oral-presentations-at-64th-ash-annual-meeting-301699713.html

SOURCE Syndax Pharmaceuticals, Inc.