Syndax Announces Revumenib Abstracts to Be Presented at the 66th ASH Annual Meeting

November 5, 2024

– New monotherapy and combination data in acute leukemia further highlight revumenib's compelling clinical profile –

– 64% ORR (62/97) in expanded dataset of patients with R/R KMT2Ar acute leukemia in Ph 2 AUGMENT-101 pivotal cohort –

– 88% ORR (23/26) in SAVE trial testing revumenib, venetoclax and decitabine/cedazuridine combination in R/R AML –

WALTHAM, Mass., Nov. 5, 2024 /PRNewswire/ -- Syndax Pharmaceuticals (Nasdaq:SNDX) today announced that multiple abstracts evaluating revumenib, an oral small molecule menin inhibitor, have been accepted for oral presentation at the 66th American Society of Hematology (ASH) Annual Meeting being held in San Diego, California, December 7-10, 2024. The oral presentations will highlight data evaluating the safety and efficacy of revumenib as monotherapy or in combination for the treatment of patients with acute leukemias.

Copies of the abstracts are now available online on the ASH website.

"The data being presented this year at ASH demonstrate Syndax's commitment to develop revumenib as a practice-changing therapy for adult and pediatric patients with acute leukemias," said Neil Gallagher, M.D., Ph.D., President, Head of Research and Development at Syndax. "We look forward to presenting these data and continuing to rapidly advance the development of revumenib for adult and pediatric acute leukemia patients who may respond to menin inhibition, such as patients with KMT2Ar or mNPM1 alterations."

The FDA has granted Priority Review for the New Drug Application (NDA) for revumenib for the treatment of adult and pediatric patients with relapsed or refractory (R/R) KMT2A-rearranged (KMT2Ar) acute leukemia. The NDA is being reviewed under the FDA's Real-Time Oncology Review Program (RTOR) and has a Prescription Drug User Fee Act (PDUFA) target action date of December 26, 2024.

In March 2024, the Company announced the completion of enrollment in the final AUGMENT-101 pivotal trial cohort in patients with R/R mutant nucleophosmin (mNPM1) acute myeloid leukemia (AML). Topline data is expected in the fourth quarter of 2024 and could support a supplemental NDA filing for revumenib in R/R mNPM1 AML in the first half of 2025.

The Company will host an in-person investor event, along with a live webcast, to discuss the latest data supporting the Company's pipeline on Monday, December 9, 2024 at 7:00 a.m. PT/ 10:00 a.m. ET during the ASH Annual Meeting. The live webcast will be available on the Investor section of the Company's website at www.syndax.com, where a replay of the event will also be available for a limited time.

Overview of Abstracts Accepted for Presentation at 66th ASH Annual Meeting

New Data from Phase 2 Portion of the AUGMENT-101 Trial of Revumenib in R/R KMT2Ar Acute Leukemia

Syndax previously presented positive data from the protocol-defined interim analysis of the pivotal Phase 2 portion of the AUGMENT-101 trial of revumenib in adult and pediatric patients with R/R KMT2Ar AML and acute lymphoid leukemia (ALL). The trial met its primary endpoint at the protocol-defined interim analysis with a complete remission (CR) or a CR with partial hematological recovery (CRh) rate of 23% (13/57; 95% CI: 12.7-35.8; one-sided p-value = 0.0036) among the 57 efficacy evaluable patients in the KMT2Ar cohort as of the July 2023 data cutoff (DCO) date.

This updated analysis (DCO: February 2024) includes 116 patients in the Phase 2 safety population (an increase of 22 patients who were enrolled and treated with revumenib after the previous July 2023 DCO), and 97 patients in the Phase 2 efficacy population (an increase of 40 patients who were newly enrolled or who reached sufficient follow-up after the previous July 2023 DCO).

Within this larger efficacy population of patients with R/R KTM2Ar acute leukemia from the Phase 2 portion of the AUGMENT-101 trial (n=97), 23% (22/97) of patients achieved CR/CRh (95% CI: 15%-32%). The CRc rate was 42% (95% CI: 32%-53%) and the ORR was 64% (95% CI: 54%-73%). Among patients with measurable residual disease (MRD) results available, 61% (11/18) of CR/CRh responders and 58% (21/36) of CRc responders achieved MRD negativity. Of the 62 patients who achieved ORR, 34% (21/62) proceeded to hematopoietic stem cell transplantation (HSCT). Nine patients resumed revumenib post-HSCT.

The median duration of response among the 22 CR/CRh responders was 6.4 months (95% CI: 1.9 mo-NR). Of note, among the 13 CR/CRh responders from the interim analysis, the median duration of CR/CRh extended to 13.0 months (95% CI: 3.4 mo–NR) after seven additional months of follow-up (DCO: February 2024). Five of these patients remained in follow-up with no relapse or death as of the data cutoff.

Within the larger safety population of patients with R/R KTM2Ar acute leukemia from the Phase 2 portion of the AUGMENT-101 trial (n=116), revumenib was generally well tolerated and the safety profile was consistent with the Company's previously reported data. Treatment-emergent adverse events (TEAEs) and treatment-related adverse events (TRAEs) leading to treatment discontinuation were low at 14% (16/116) and 5% (6/116), respectively. The most common Grade ≥3 TEAEs were consistent with previously reported data. Grade 3 treatment-emergent differentiation syndrome (DS) was observed in 14% (16/116) of patients and one patient (1%) experienced a Grade 4 DS. Grade 3 treatment-emergent QTc prolongation was observed in 13% (15/116) of patients, with no Grade 4 or Grade 5 events.

Details for the oral presentation are as follows:

Abstract Number: 211
Title: Updated Results and Longer Follow-up from the AUGMENT-101 Phase 2 Study of Revumenib in All Patients with Relapsed or Refractory (R/R) KMT2Ar Acute Leukemia
Presenter: Ibrahim Aldoss, M.D.
Session Name: 616. Acute Myeloid Leukemias: Investigational Drug and Cellular Therapies: Menin Inhibitors in AML
Session Date: Saturday, December 7, 2024
Session Time: 2:00 PM - 3:30 PM
Presentation Time: 2:00 PM

New Results from Phase 1/2 SAVE Trial of Revumenib in Combination with Venetoclax and Decitabine/Cedazuridine in R/R AML

The Phase 1/2 SAVE trial is an investigator-sponsored trial testing an all-oral regimen of revumenib, venetoclax and the hypomethylating agent (HMA) ASTX727 (decitabine/cedazuridine) in children and adults with R/R AML or mixed-lineage acute leukemia (MPAL) harboring either KMT2Ar, NUP98r or mNPM1 alterations.

As of the latest data cutoff (July 2024), 26 patients were enrolled in the trial. The median age was 35 years (range: 12-79). At baseline, 11 patients (42%) had KMT2Ar, 10 patients (38%) had mNPM1, and five patients (20%) had NUP98r. The median prior lines of therapy was three (range: 1-5); 17 patients (65%) had prior venetoclax, 11 (42%) had prior HSCT, and two had received a prior menin inhibitor.

The all-oral combination resulted in high rates of remission in patients with R/R KMT2Ar, mNPM1, or NUP98r AML. The ORR was 88% (23/26), with a CR/CRh rate of 58% (15/26). MRD status was available in 14 of the 15 patients who achieved a CR/CRh, 93% (13/14) of whom were MRD negative. In patients with MRD status available who achieved a response, 74% (17/23) were MRD negative. Twelve patients (46%) received HSCT following this combination, with three patients resuming revumenib post-HSCT.

With a median follow-up of 6.6 months, the 6-month relapse-free survival was 59% (95% CI: 26%-81%) and overall survival was 74% (95% CI: 39%-83%). The median duration of response in those with CR/CRh was not reached. Two patients had completed maintenance post-HSCT and remained in remission at the time of the data cutoff.

The combination was generally well tolerated. The most common (>20%) Grade ≥3 TEAEs were febrile neutropenia (46%) and lung infection (42%), while Grade ≥3 TRAEs (any agent) were thrombocytopenia (12%), neutropenia (8%), QT prolongation (8%), and DS (4%). No patient experienced Grade 4 or 5 DS, and all DS events were resolved with steroids.

In addition to the R/R cohort, a frontline cohort is now enrolling patients.

Details for the oral presentation are as follows:

Abstract Number: 216
Title: Phase I/II Study of the All-Oral Combination of Revumenib (SNDX-5613) with Decitabine/Cedazuridine (ASTX727) and Venetoclax (SAVE) in R/R AML
Presenter: Ghayas C. Issa, M.D.
Session Name: 616. Acute Myeloid Leukemias: Investigational Drug and Cellular Therapies: Menin Inhibitors in AML
Session Date: Saturday, December 7, 2024
Session Time: 2:00 PM - 3:30 PM
Presentation Time: 3:15 PM

Initial Results from INTERCEPT Trial of Revumenib as Pre-Emptive Therapy for MRD Positive AML

INTERCEPT is an investigator-sponsored platform trial evaluating the use of novel therapies, including revumenib, to target MRD and early relapse in AML. This proof-of-concept trial is exploring whether targeting MRD in patients with progressive AML may be an effective approach to maintaining patients in first (CR1) or second remission (CR2).

As of the July 2024 data cut off, nine patients with MRD relapse (eight with mNPM1 and one with KMT2Ar) were enrolled in the safety cohort and received revumenib. The median age was 62 years; seven were in CR1, two in CR2; three had prior venetoclax exposure and six had prior intensive therapy.

In a preliminary analysis of the eight mNPM1 patients who received revumenib, five of the eight patients had MRD reduction, including three who achieved MRD negativity within six cycles. In the nine-patient safety cohort, dose-limiting toxicities included reversible Grade 3 QTc prolongation in two patients; neither de-escalation nor elimination were mandated and 276 mg of revumenib BID was therefore considered safe for further expansion. These data support revumenib's safety profile and activity in patients with mNPM1 MRD relapse.

Details for the oral presentation are as follows:

Abstract Number: 223
Title: Revumenib as Pre-emptive Therapy for Measurable Residual Disease in NPM1 mutated or KMT2A-rearranged Acute Myeloid Leukemia: A Domain of the Multi-Arm ALLG AMLM26 Intercept Platform trial
Presenter: Sun Loo, M.B.B.S.
Session Name: 619. Acute Myeloid Leukemias: Disease Burden and Minimal Residual Disease in Prognosis and Treatment: Measurable Residual Disease in AML in 2024 and Beyond
Session Date: Saturday, December 7, 2024
Session Time: 2:00 PM - 3:30 PM
Presentation Time: 2:00 PM

About Revumenib
Revumenib is an oral, small molecule inhibitor of the menin-KMT2A binding interaction that is being developed for the treatment of KMT2A-rearranged (KMT2Ar), also known as mixed lineage leukemia rearranged or MLLr, acute leukemias including acute lymphoid leukemia (ALL) and acute myeloid leukemia (AML), and mutant NPM1 AML. The *Journal of Clinical Oncology* published results from the Phase 2 AUGMENT-101 trial of revumenib in R/R KMT2Ar acute leukemia showing the trial met its primary endpoint.

Revumenib was previously granted Orphan Drug Designation for the treatment of AML, ALL and acute leukemias of ambiguous lineage (ALAL) by the U.S. FDA and for the treatment of AML by the European Commission. The U.S. FDA also granted Fast Track designation to revumenib for the treatment of adult and pediatric patients with R/R acute leukemias harboring a KMT2A rearrangement or NPM1 mutation and Breakthrough Therapy Designation for the treatment of adult and pediatric patients with R/R acute leukemia harboring a KMT2A rearrangement.

About Syndax
Syndax Pharmaceuticals is a commercial-stage biopharmaceutical company developing an innovative pipeline of cancer therapies. Highlights of the Company's pipeline include revumenib, a selective menin inhibitor, and Niktimvo™ (axatilimab-csfr), an FDA-approved monoclonal antibody that blocks the colony stimulating factor 1 (CSF-1) receptor. Fueled by our commitment to reimagining cancer care, Syndax is working to unlock the full potential of its pipeline and is conducting several clinical trials across the continuum of treatment. For more information, please visit www.syndax.com/ or follow the Company on X (formerly Twitter) and LinkedIn.

Syndax 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 acceptance of Syndax and its partners' products in the marketplace, sales, marketing, manufacturing and distribution requirements, 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; 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.

References

[1] Overall response rate includes CR, CRh, CRp, CRi, MLFS, and PR; Composite complete remission (CRc) includes CR, CRh, CRp, and CRi
CR = Complete remission
CRh = Complete remission with partial hematologic recovery
CRp = Complete remission with incomplete platelet recovery
CRi = Complete remission with incomplete count recovery
MLFS = Morphologic leukemia-free state
PR = Partial response

Syndax Contact:
Sharon Klahre
sklahre@syndax.com
Tel 781.684.9827

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