Syndax Presents Updated Positive Data from BEAT AML and AUGMENT-102 Phase 1/2 Combination Trials of Revumenib in Patients with Acute Leukemias at EHA 2024 Congress

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- Data continue to support revumenib's potential to enhance current standard of care agents -

- 96% CRc (23 of 24 pts) observed in BEAT AML trial exploring revumenib in combination with venetoclax/azacitidine in newly diagnosed mNPM1 or KMT2Ar AML -

- 52% CRc (14 of 27 pts) observed in AUGMENT-102 trial of revumenib in combination with fludarabine-cytarabine in acute leukemia patients with R/R mNPM1, NUP98r or KMT2Ar -

WALTHAM, Mass., June 14, 2024 /PRNewswire/ -- Syndax Pharmaceuticals (Nasdaq: SNDX), a clinical stage biopharmaceutical company developing an innovative pipeline of cancer therapies, today announced updated data from multiple combination trials of revumenib, the Company's potent, selective, small molecule menin inhibitor, in patients with acute leukemias. The updated data are being presented at the European Hematology Association (EHA) 2024 Congress, being held June 13-16 in Madrid, Spain and virtually.

"The growing body of data supports the potential for revumenib to have a meaningful impact in combination with current standard of care therapies," said Joshua F. Zeidner, M.D., Chief, Leukemia Research at the University of North Carolina, Lineberger Comprehensive Cancer Center. "Based on the BEAT AML data in the newly diagnosed setting which showed a high rate of MRD-negative responses coupled with a safety profile that enables combination use, revumenib has the potential to become a cornerstone of treatment as front-line therapy for newly diagnosed KMT2Ar and mNPM1 AML."

"We are committed to advancing revumenib across a spectrum of acute leukemia patients. As we prepare for the expected near-term approval of revumenib in the relapsed or refractory setting, we look forward to providing additional clinical data as monotherapy and in combination to support treatment in various acute leukemia treatment settings where novel treatment options are urgently needed," said Neil Gallagher, M.D., Ph.D., President, Head of Research and Development at Syndax.

BEAT AML Trial

The Company announced updated data from the BEAT AML trial of revumenib in combination with venetoclax/azacitidine in newly diagnosed mutant nucleophosmin (mNPM1) or KMT2A-rearranged (KMT2Ar) acute myeloid leukemia (AML) patients aged 60 years or older in an oral presentation titled "Phase 1b Study of Azacitidine, Venetoclax and Revumenib in Newly Diagnosed Older Adults with NPM1 Mutated or KMT2A Rearranged AML: Interim Results of Dose Escalation from the BeatAML Consortium."

The dose escalation phase of the trial tested revumenib at doses of 113 mg and 163 mg q12h in combination with a strong CYP3A4 inhibitor beginning on day 1 of a 28-day cycle in combination with on label doses of venetoclax and azacitidine. As of the data cutoff date of May 1, 2024, 26 newly diagnosed mNPM1 (n=17) or KMT2Ar (n=9) AML patients were enrolled. In the efficacy evaluable population, the composite complete remission[1] (CRc) rate was 96% (23/24) and 92% (22/24) of patients also attained minimal residual disease (MRD) negative status as determined by central flow cytometry. Three patients proceeded to hematopoietic stem cell transplant (HSCT). The first cohort of patients treated in the trial, at 113 mg, had extended follow-up and an estimated 12-month survival of 100%.

Revumenib was dosed safely at both the 113 mg and 163 mg q12h dose in combination with venetoclax and azacitidine. 15% (4/26) of patients experienced differentiation syndrome with one (4%) Grade 3 event. 46% (12/26) of patients experienced QTc prolongation with three (12%) Grade 3 events. All DS and QTc prolongations were self-limiting and resolved without complication or the need for revumenib dose reductions. Venetoclax was dosed in accordance with its label and an analysis of the onset and extent of hematologic toxicities suggest a similar experience to what has been reported for the venetoclax/azacytidine doublet. Overall, there were no new or increased safety signals observed when revumenib was added to this triplet combination.

An expansion cohort is ongoing at both dose levels to establish the recommended dose for future trials. The Company plans to initiate a pivotal trial with this combination in front-line newly diagnosed patients by year-end 2024.

AUGMENT-102 Trial

The Company also announced a poster presentation featuring updated data from the AUGMENT-102 trial of revumenib in combination with fludarabine/cytarabine in a predominantly pediatric population of patients with relapsed/refractory (R/R) mNPM1 (n=2), NUP98-rearranged (NUP98r) (n=1) or KMT2Ar (n=23) AML titled "Safety and Activity of Revumenib in Combination with Fludarabine/Cytarabine (FLA) in Patients with Relapsed/Refractory Acute Leukemias."

As of the data cutoff date of January 15, 2024, 27 patients received revumenib plus FLA, including 9 patients treated at 113 mg q12h and 18 treated at 163 mg q12h. The patients enrolled had a median age of 6 years and had received a median of 3 prior lines of therapy. Eighteen (67%) patients had prior FLA containing regimens while 11 (41%) patients had prior HSCT. Five (56%) patients treated at the 113 mg q12h dose and nine (50%) patients treated at the 163 mg q12h achieved a CRc. Most patients who achieved a CRc and had evaluable data achieved (MRD) negative status (10/14; 71%) and 7 patients underwent HSCT while in remission following treatment.

Overall, revumenib was tolerable in heavily pretreated patients with *KMT2Ar*, *NUP98r*, or *NPM1m* acute leukemias without increased frequency or severity of AEs compared with historic FLA data or revumenib monotherapy. One DLT occurred at the 163 mg q12h dose that was a Grade 4 decreased neutrophil count in a patient with multiple prior transplants.

Grade 3 and above adverse events in over 40% of patients included decreased platelet count (17/27; 63%), anemia (15/27; 56%) and febrile neutropenia (13/27; 48%). Lower rates of cytopenias were reported at the 163 mg q12h dose than the 113 mg q12h dose, consistent with faster remission at the higher dose. Lower rates of nonhematologic adverse events were also observed at the higher dose level, which further suggests that the adverse event profile was not driven by revumenib. There was one adverse event leading to death (sepsis at the 113 mg q12h dose level) not

related to revumenib. There were no cases of differentiation syndrome in the trial.

This study supports the selection of revumenib 163 mg q12h (95 mg/m2 q12h if weight <40 kg) combined with FLA and a strong cytochrome P450 inhibitor as the RP2D, in line with the dose of revumenib under FDA review as a monotherapy agent.

Additional Presentations at EHA 2024

In addition to updated results from the BEAT AML and AUGMENT-102 studies, an encore presentation of results from the pivotal AUGMENT-101 study of revumenib in R/R KMT2Ar acute leukemia were also featured at the Congress during an oral session titled "Revumenib Monotherapy in Patients with Relapsed/Refractory KMT2Ar Acute Leukemia: Topline Efficacy and Safety Results from the Pivotal AUGMENT-101 Phase 2 Study."

Results from an exploratory analysis of immunophenotypic changes in AML blasts following treatment with revumenib were also featured in a poster presentation titled "Characterization of Immunophenotypic Changes Following Menin Inhibition in Acute Myeloid Leukemia."

Copies of EHA posters and presentations will be available in the Publications and Meeting Presentations section of Syndax's website.

About Revumenib

Revumenib is a potent, selective, 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 ALL and AML, and mutant nucleophosmin (mNPM1) AML. Positive topline results from the Phase 2 AUGMENT-101 trial in R/R KMT2Ar acute leukemia showing the trial met its primary endpoint were presented at the 65th American Society of Hematology Annual Meeting, and data from the Phase 1 portion of AUGMENT-101 in acute leukemia was published in Nature. Revumenib was granted Orphan Drug Designation by the 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 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 Syndax

Syndax Pharmaceuticals is a clinical stage biopharmaceutical company developing an innovative pipeline of cancer therapies. Highlights of the Company's pipeline include revumenib, a highly selective menin inhibitor, and axatilimab, a monoclonal antibody that blocks the CSF-1 receptor. For more information, please visit www.syndax.com or follow the Company on X (formerly 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 "anticipate," "believe," "could," "estimate," "expects," "intend," "may," "plan," "potential," "predict," "project," "should," "will," "would" or the negative or plural of those terms, 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 its 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]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

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