Syndax Announces Additional Positive Data for Revuforj® (revumenib) from AUGMENT-101 Trial in Relapsed or Refractory mNPM1 AML and BEAT AML Frontline Combination Trial

December 9, 2024

– Subgroup analyses from Ph 2 protocol-defined R/R mNPM1 AML efficacy population (N=64) show responses across all major subgroups, including heavily pretreated patients –

– 26% CR+CRh (20/77) and 48% ORR (37/77) in all enrolled patients who met the efficacy evaluable criteria in Ph 2 R/R mNPM1 AML cohort –

– 100% ORR (37/37) and 95% CRc (35/37) in BEAT AML trial exploring revumenib in combination with venetoclax/azacitidine in newly diagnosed mNPM1 or KMT2Ar AML –

– BEAT AML data highlight the potential for revumenib to advance the current standard of care –

WALTHAM, Mass., Dec. 9, 2024 /PRNewswire/ -- Syndax Pharmaceuticals (Nasdaq: SNDX), a commercial-stage biopharmaceutical company developing an innovative pipeline of cancer therapies, today announced additional positive data from the AUGMENT-101 trial of Revuforj® (revumenib) in relapsed or refractory (R/R) mutant NPM1 (mNPM1) acute myeloid leukemia (AML) and the BEAT AML trial of revumenib in combination with venetoclax and azacitidine in newly diagnosed AML patients. Revuforj is the Company's oral, first-in-class menin inhibitor that is FDA approved for the treatment of relapsed or refractory (R/R) acute leukemia with a lysine methyltransferase 2A gene (KMT2A) translocation in adult and pediatric patients one year and older.

"These new data continue to highlight the exciting potential for Revuforj as both a monotherapy and in combination with other therapies," said Michael A. Metzger, Chief Executive Officer of Syndax. "The recent approval of Revuforj for R/R acute leukemia with a KMT2A translocation, coupled with the consistency of the results we have reported across KMT2Ar and mNPM1 within the different trials and populations, continues to bolster our confidence in its practice-changing and blockbuster potential."

Additional Results from R/R mNPM1 AML Patients in Pivotal Phase 2 Portion of AUGMENT-101

Syndax recently announced that the primary endpoint was met with a complete remission (CR) plus CR with partial hematological recovery (CRh) rate of 23% (15/64; 95% confidence interval [CI]: 14%, 36%; one-sided p-value =0.0014) in the protocol-defined efficacy population of 64 adults with R/R mNPM1 AML in the Phase 2 cohort of the AUGMENT-101 trial of revumenib (DCO: September 2024). The median duration of CR/CRh responses was 4.7 months at the time of the data cutoff with three patients remaining in response. Minimal residual disease (MRD) status was assessed in 14 of 15 patients who achieved CR/CRh, 64% (9/14) of whom were MRD negative. The overall response rate (ORR)[1] was 47% (30/64). The safety profile observed with revumenib in the 84 patients enrolled in the cohort was consistent with previously reported data.

Syndax announced today additional results from the Phase 2 cohort of R/R mNPM1 AML patients in the AUGMENT-101 trial, including data generated from the protocol-defined efficacy population of 64 adults and a post-hoc efficacy analysis based on all patients who met the efficacy evaluable criteria.

Subgroup analyses from the Phase 2 protocol-defined R/R mNPM1 efficacy population (N=64) show that CR/CRh responses were observed across all major subgroups, including patients with multiple prior lines of therapy and prior venetoclax exposure, although the trial was not powered to evaluate differences among subgroups. The CR+CRh rate was 25% (4/16) among patients with 1 prior line of therapy, 20% (5/25) among patients with 2 prior lines of therapy, and 26% (6/23) among patients who had received three or more prior lines of therapy. The CR+CRh rate was 44% (7/16) among patients without prior venetoclax exposure and 17% (8/48) among patients with prior venetoclax exposure. Historically, AML patients who have failed prior treatment with venetoclax are unlikely to respond to subsequent therapy, with a CR rate of 6% reported for other targeted therapies after prior venetoclax therapy.[2]

Syndax also shared results from an expanded analysis of the R/R mNPM1 AML patients who enrolled into the Phase 2 cohort of AUGMENT-101. Among the 84 patients enrolled in the cohort, 77 met the efficacy evaluable criteria requiring patients to have blast counts >5% measured within 28 days prior to treatment and a centrally confirmed NPM1 mutation. In this expanded post-hoc efficacy analysis, 48% (37/77; 95% CI: 37%, 60%) achieved an overall response, and 26% (20/77; 95% CI: 17%, 37%) achieved a CR/CRh. The median duration of CR/CRh response was 4.7 months as of the September 2024 DCO. Minimal residual disease (MRD) status was assessed in 19 of 20 patients who achieved CR/CRh, 63% (12/19) of whom were MRD negative.

Updated Data from BEAT-AML Trial of Revumenib in Combination with Venetoclax and Azacitidine in Newly Diagnosed AML Patients

Today the company announced an update from the Phase 1 BEAT-AML trial evaluating the combination of revumenib with venetoclax and azacitidine in newly diagnosed mNPM1 or KMT2A-rearranged (KMT2Ar) AML patients aged 60 years or older. The trial is being conducted as part of the Leukemia & Lymphoma Society's Beat AML® Master Clinical Trial. Today's update builds on the BEAT AML data that was presented in June at the European Hematology Association (EHA) 2024 Congress from 24 efficacy evaluable patients showing a composite complete remission (CRc) rate of 96% (23/24) as of a May 2024 data cutoff.

As of a November 2024 data cutoff, 46 newly diagnosed mNPM1 (n=37) or KMT2Ar (n=9) patients have been enrolled in BEAT AML across two dose levels of revumenib (113 mg q12 or 163 mg q12h with azoles) in combination with venetoclax and azacitidine. The median age of patients enrolled was 71 years (range: 60-92).

The efficacy evaluable population includes 37 patients across both dose levels with an ORR[1] of 100% (37/37) and CRc rate of 95% (35/37). The rate of MRD negativity was 95% (35/37). 27% (10/37) of patients proceeded to hematopoietic stem cell transplant (HSCT).

Revumenib was generally well tolerated at both the 113 mg and 163 mg q12h dose in combination with venetoclax and azacitidine. In the safety population (N=46), 15% (7/46) of patients experienced differentiation syndrome with two (4%) Grade 3 or greater events. 43% (20/46) of patients experienced QTc prolongation with five (11%) Grade 3 or greater events. DS and QTc prolongations were self-limiting and did not cause any

discontinuations. Analysis of the onset and extent of hematologic toxicities suggest a similar experience to what has been reported for the venetoclax/azacitidine doublet alone. Overall, there were no new or increased safety signals observed when revumenib was included in this triplet combination.

"These are very exciting data that highlight the potential for revumenib to enhance the responses typically observed with venetoclax/azacitidine in newly diagnosed patients with mNPM1 or KMT2Ar who are unfit to receive intensive chemotherapy," said Joshua F. Zeidner, M.D., Chief, Leukemia Research at the University of North Carolina, Lineberger Comprehensive Cancer Center. "These new data continue to show that revumenib has a safety profile that could enable it to be combined with venetoclax/azacitidine and, importantly, we are observing high rates of response and MRD negativity that underscore the potential for revumenib to become an integral component of frontline treatment for KMT2Ar and mNPM1 AML patients."

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

Syndax Corporate Event

The new data described above, along with other data presented through today at the 66th ASH Annual Meeting being held in San Diego, CA for both the Revuforj (revumenib) and Niktimvo (axatilimab-csfr) clinical programs, will be highlighted at the Company's investor event on Monday, December 9, 2024 at 7:00 a.m. PT/10:00 a.m. ET. The live audio webcast and accompanying slides for the event may be accessed through the Events & Presentations page in the Investors section of the Company's website or directly through the meeting link here.

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

About Revuforj® (revumenib)

Revuforj (revumenib) is an oral, first-in-class menin inhibitor that is FDA approved for the treatment of relapsed or refractory (R/R) acute leukemia with a lysine methyltransferase 2A gene (KMT2A) translocation in adult and pediatric patients one year and older.

Revumenib is in development for the treatment of R/R acute myeloid leukemia (AML) with a nucleophosmin 1 mutation (mNPM1). Positive pivotal data from the AUGMENT-101 trial in this population with revumenib as a monotherapy were recently reported. The Company expects to file a supplemental NDA filing for revumenib in R/R mNPM1 AML in the first half of 2025. Additionally, multiple trials of revumenib in combination with standard-of-care agents in mNPM1 AML or KMT2A-rearranged acute leukemia are ongoing across the treatment landscape, including in newly diagnosed patients.

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.

IMPORTANT SAFETY INFORMATION

WARNING: DIFFERENTIATION SYNDROME

Differentiation syndrome, which can be fatal, has occurred with Revuforj. Signs and symptoms may include fever, dyspnea, hypoxia, pulmonary infiltrates, pleural or pericardial effusions, rapid weight gain or peripheral edema, hypotension, and renal dysfunction. If differentiation syndrome is suspected, immediately initiate corticosteroid therapy and hemodynamic monitoring until symptom resolution.

WARNINGS AND PRECAUTIONS

Differentiation syndrome: Revuforj can cause fatal or life-threatening differentiation syndrome (DS). Symptoms of DS, including those seen in patients treated with Revuforj, include fever, dyspnea, hypoxia, peripheral edema, pleuropericardial effusion, acute renal failure, and/or hypotension. In clinical trials, DS occurred in 39 (29%) of 135 patients treated with Revuforj. DS was Grade 3 or 4 in 13% of patients and fatal in one. The median time to onset was 10 days (range 3-41 days). Some patients experienced more than 1 DS event. Treatment interruption was required for 7% of patients, and treatment was withdrawn for 1%.

Reduce the white blood cell count to less than 25 Gi/L prior to starting Revuforj. If DS is suspected, immediately initiate treatment with systemic corticosteroids (e.g., dexamethasone 10-mg IV every 12 hours in adults or dexamethasone 0.25-mg/kg/dose IV every 12 hours in pediatric patients weighing less than 40 kg) for a minimum of 3 days and until resolution of signs and symptoms. Institute supportive measures and hemodynamic monitoring until improvement. Interrupt Revuforj if severe signs and/or symptoms persist for more than 48 hours after initiation of systemic corticosteroids, or earlier if life-threatening symptoms occur such as pulmonary symptoms requiring ventilator support. Restart steroids promptly if DS recurs after tapering corticosteroids.

QTc interval prolongation: In the clinical trials, QTc interval prolongation was reported as an adverse reaction in 39 (29%) of 135 patients treated with Revuforj. QTc interval prolongation was Grade 3 in 12% of patients. The heart-rate corrected QT interval (using Fridericia's method) (QTcF) was greater than 500 msec in 8%, and the increase from baseline QTcF was greater than 60 msec in 18%. Revuforj dose reduction was required for 5% of patients due to QTc interval prolongation. QTc prolongation occurred in 16% of the 31 patients less than 17 years old, 33% of the 88 patients 17 years to less than 65 years old, and in 50% of the 16 patients 65 years or older.

Correct electrolyte abnormalities, including hypokalemia and hypomagnesemia, prior to treatment with Revuforj. Perform an electrocardiogram (ECG) prior to initiation of Revuforj, and do not initiate Revuforj in patients with QTcF >450 msec. Perform an ECG at least once weekly for the first 4 weeks and at least monthly thereafter. In patients with congenital long QTc syndrome, congestive heart failure, electrolyte abnormalities, or those who are taking medications known to prolong the QTc interval, more frequent ECG monitoring may be necessary. Concomitant use with drugs known to prolong the QTc interval may increase the risk of QTc interval prolongation.

- Interrupt Revuforj if QTcF increases >480 msec and <500 msec, and restart Revuforj at the same dose twice daily after the QTcF interval returns to ≤480 msec
- Interrupt Revuforj if QTcF increases >500 msec or by >60 msec from baseline, and restart Revuforj twice daily at the lower-dose level after the QTcF interval returns to ≤480 msec
- Permanently discontinue Revuforj in patients with ventricular arrhythmias and in those who develop QTc interval prolongation with signs or symptoms of life-threatening arrhythmia.

Embryo-fetal toxicity: Revuforj can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential and males with female partners of reproductive potential to use effective contraception during treatment with Revuforj and for 4 months after the last dose of Revuforj.

ADVERSE REACTIONS
Fatal adverse reactions occurred in 4 (3%) patients who received Revuforj, including 2 with differentiation syndrome, 1 with hemorrhage, and 1 with sudden death.

Serious adverse reactions were reported in 99 (73%) patients. The most frequent **serious adverse reactions** (≥5%) were infection (24%), febrile neutropenia (19%), bacterial infection (17%), differentiation syndrome (12%), hemorrhage (9%), and thrombosis (5%).

The most **common adverse reactions** (≥20%) including laboratory abnormalities, were hemorrhage (53%), nausea (51%), phosphate increased (50%), musculoskeletal pain (42%), infection (41%), aspartate aminotransferase increased (37%), febrile neutropenia (35%), alanine aminotransferase increased (33%), parathyroid hormone intact increased (33%), bacterial infection (31%), diarrhea (30%), differentiation syndrome (29%), electrocardiogram QT prolonged (29%), phosphate decreased (25%), triglycerides increased (25%), potassium decreased (24%), decreased appetite (24%), constipation (23%), edema (23%), viral infection (23%), fatigue (22%), and alkaline phosphatase increased (21%).

DRUG INTERACTIONS
Drug interactions can occur when Revuforj is concomitantly used with:

- Strong CYP3A4 inhibitors: reduce Revuforj dose
- Strong or moderate CYP3A4 inducers: avoid concomitant use with Revuforj
- QTc-prolonging drugs: avoid concomitant use with Revuforj. If concomitant use is unavoidable, obtain ECGs when initiating, during concomitant use, and as clinically indicated. Withhold Revuforj if the QTc interval is >480 msec. Restart Revuforj after the QTc interval returns to ≤480 msec.

SPECIFIC POPULATIONS
Lactation: advise lactating women not to breastfeed during treatment with Revuforj and for 1 week after the last dose.

Pregnancy and testing: Revuforj can cause fetal harm when administered to a pregnant woman. Verify pregnancy status in females of reproductive potential within 7 days prior to initiating Revuforj.

Pediatric: monitor bone growth and development in pediatric patients.

Geriatric: compared to younger patients, the incidences of QTc prolongation and edema were higher in patients 65 years and older.

Infertility: based on findings in animals, Revuforj may impair fertility. The effects on fertility were reversible.

To report SUSPECTED ADVERSE REACTIONS, contact Syndax Pharmaceuticals at 1-888-539-3REV or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see Full Prescribing Information, including BOXED WARNING.

About Syndax

Syndax Pharmaceuticals is a commercial-stage biopharmaceutical company developing an innovative pipeline of cancer therapies. Highlights of the Company's pipeline include Revuforj® (revumenib), an FDA-approved 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.

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, the acceptance of Syndax and its partners' products in the marketplace, sales, marketing, manufacturing and distribution requirements, 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 to Revuforj's commercial availability, 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 (ORR) 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

2. Bewersdorf JP, Shallis RM, Derkach A, et al. Efficacy of FLT3 and IDH1/2 inhibitors in patients with acute myeloid leukemia previously treated with venetoclax. Leuk Res. 2022;122:106942. doi:10.1016/j.leukres.2022.106942

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