Syndax Announces Publication of Revumenib Data from the BEAT AML Trial in the Journal of Clinical Oncology and Simultaneous Presentation at EHA 2025

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– Revumenib was generally well-tolerated in combination with venetoclax/azacitidine in older, newly diagnosed mNPM1 and KMT2Ar AML patients –

– Promising clinical activity and deep responses observed with 67% (29/43) CR rate, 88% (38/43) ORR, and 100% (37/37) MRD negativity among responders –

– Enrollment underway in pivotal Ph 3 EVOLVE-2 trial evaluating revumenib with ven/aza in newly diagnosed mNPM1 AML patients unfit for intensive chemotherapy –

NEW YORK, June 12, 2025 (GLOBE NEWSWIRE) -- Syndax Pharmaceuticals (Nasdaq: SNDX), a commercial-stage biopharmaceutical company advancing innovative cancer therapies, today announced that data from the BEAT AML trial of revumenib in combination with venetoclax and azacitidine (ven/aza) in newly diagnosed mutant NPM1 (mNPM1) and KMT2A-rearranged (KMT2Ar) acute myeloid leukemia (AML) patients were published in the *Journal of Clinical Oncology* and simultaneously presented in an oral session at the 30th European Hematology Association (EHA) Annual Congress Meeting being held June 12-15, 2025, in Milan, Italy and virtually.

“The data observed in BEAT AML underscore the potential for revumenib with ven/aza to improve outcomes for newly diagnosed mNPM1 or KMT2Ar AML patients who are not eligible for intensive chemotherapy, a population that continues to face poor long-term outcomes despite recent advances,” said Nick Botwood, M.B.B.S., Head of Research & Development and Chief Medical Officer at Syndax. “These data, along with the results from other trials of revumenib in different settings, highlight revumenib’s potential to become a cornerstone therapy for all menin-dependent acute leukemias across the treatment continuum.”

“These data support the ability to combine revumenib with ven/aza in the frontline setting and the clinical activity observed highlights the potential for the triplet to provide high rates of complete remission and MRD-negativity, two treatment goals associated with improved clinical outcomes,” said Joshua F. Zeidner, M.D., Chief, Leukemia Research at the University of North Carolina, Lineberger Comprehensive Cancer Center and Principal Investigator in the BEAT AML trial. “Overall, the data we observed in BEAT AML are very encouraging and suggest that the ongoing EVOLVE-2 pivotal frontline trial evaluating the triplet in unfit mNPM1 AML patients could deliver practice-changing results.”

Summary of Results from BEAT AML Phase 1 Trial

The publication and EHA presentation report updated results from the Phase 1b BEAT AML trial evaluating the safety and clinical activity of revumenib in combination with venetoclax/azacitidine in newly diagnosed older adults (≥60 years) with mNPM1 or KMT2Ar AML. The trial is being conducted as part of The Leukemia & Lymphoma Society's Beat AML® Master Clinical Trial (NCT03013998).

As of September 2024, 43 patients were enrolled and treated in BEAT AML across two dose levels of revumenib (113 mg q12 or 163 mg q12h with strong CYP3A4 inhibitor azoles) in combination with venetoclax and azacitidine. Overall, 79% (34/43) of patients had mNPM1 AML and 21% (9/43) had KMT2Ar AML. The median age was 70 years (range: 60-92) and 40% were ≥75 years.

Revumenib was generally well tolerated at both dose levels in combination with venetoclax and azacitidine without a maximal tolerated dose identified. The most common overall non-hematologic treatment-emergent adverse events (TEAEs) of any grade were nausea (60%), constipation (53%), QTc prolongation (44%), hypokalemia (44%), and vomiting (42%). Overall Grade ≥3 non-hematologic AEs were rare and similar between both dose levels.

In the intent-to-treat population, the observed rate of complete remission (CR) was 67% (29/43), composite complete remission (CRc) was 81% (35/43), and the overall response rate (ORR) was 88% (38/43). Among 37 patients with measurable residual disease (MRD) response assessment, 100% were MRD negative by centralized flow cytometry testing (sensitivity of 0.02%). The median duration of CRc was 12.0 months (95% CI: 7.8-not reached). 23% (10/43) of patients had proceeded to hematopoietic stem cell transplantation (HSCT) as of the February 2025 data cut off.

In an early analysis of survival from this single-arm trial (median follow-up of 6.9 months), the median overall survival (OS) observed was 15.5 months (95% CI: 9.5-19.5). Subset analysis showed a CRc rate of 77% and an observed median OS of 15.5 months in mNPM1 patients with intermediate risk by ELN 2024 (n=17), and a CRc rate of 89% and observed median OS of 18.0 months in KMT2Ar patients (n=9). In contrast, historical data from newly diagnosed mNPM1 patients with intermediate risk treated with venetoclax and azacitidine show a CRc of 57% and median OS of 9.9 months.[1] In newly diagnosed KMT2Ar AML patients treated with venetoclax and hypomethylating agent therapy, a CRc rate of 43% and median OS of 2.5 months was observed in a retrospective analysis.[2]

About Revuforj® (revumenib)

Revuforj (revumenib) is an oral, first-in-class, selective 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 published and the Company completed the submission of a supplemental NDA for revumenib in R/R mNPM1 AML in April 2025. Additionally, multiple trials of revumenib in combination with standard-of-care agents in mNPM1 AML or KMT2A-rearranged acute leukemia are ongoing or planned 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 advancing innovative 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 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 or Niktimvo'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. Döhner H, et al. Genetic risk stratification and outcomes among treatment-naive patients with AML treated with venetoclax and azacitidine. *Blood* 2024; 144 (21): 2211– 222.

2. Gangat N, et al. Mayo Genetic Risk Models for Newly Diagnosed Acute Myeloid Leukemia Treated With Venetoclax + Hypomethylating Agent. Am J Hematol. 2025;100(2):260-271.

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