Syndax Presents Positive Revuforj® (revumenib) Data in Acute Leukemias from Multiple Trials, Including the SAVE Combination and AUGMENT-101 Trials, at 66th ASH Annual Meeting

December 7, 2024

– 82% ORR (27 of 33 pts) and 48% CR/CRh (16 of 33 pts) in SAVE trial studying revumenib in combination with venetoclax and decitabine/cedazuridine in R/R AML –

– 64% ORR (62 of 97 pts) and 23% CR/CRh (22 of 97 pts) with high rates of MRD negativity and ability to proceed to HSCT in expanded dataset of Ph 2 R/R KMT2Ar acute leukemia patients in AUGMENT-101 –

– Responses were rapid, durable and observed across all major subgroups in expanded dataset of Ph 2 R/R KMT2Ar acute leukemia patients in AUGMENT-101 –

– Latest data highlight the compelling clinical profile of revumenib and support advancement into combination trials in the frontline setting –

WALTHAM, Mass., Dec. 7, 2024 /PRNewswire/ -- Syndax Pharmaceuticals (Nasdaq: SNDX), a commercial-stage biopharmaceutical company developing an innovative pipeline of cancer therapies, today presented positive data from multiple trials of Revuforj® (revumenib) as a single-agent and in combination with standard of care agents in patients with acute leukemias in oral sessions at the 66th American Society of Hematology (ASH) Annual Meeting being held in San Diego, December 7-10, 2024. 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.

"On the heels of the recent approval of Revuforj for R/R acute leukemia with a KMT2A translocation, we are excited to present clinical data highlighting the consistent efficacy and favorable tolerability of this first-in-class therapy, as both a single-agent and in combination with standard of care, in patients with mNPM1 and KMT2Ar acute leukemia," said Michael A. Metzger, Chief Executive Officer. "We are thrilled that our U.S. launch of Revuforj is firmly underway, and we look forward to building on this momentum as we continue to advance our clinical development program which we believe will position us to pursue meaningful label expansion opportunities."

Overview of Revumenib Data Presented in Oral Sessions at 66th ASH Annual Meeting

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 pediatric and adult patients with R/R acute myeloid leukemia (AML) or mixed-lineage acute leukemia (MPAL) harboring either KMT2Ar, NUP98r or mNPM1 alterations. In the previously announced ASH abstract, data from 26 patients in the SAVE trial were reported (data cutoff [DCO]: July 2024).

During the oral session at the ASH meeting, data from 33 patients were presented (DCO: November 2024). The median age of patients enrolled in the trial was 35 (range 12-81), and 16 patients (49%) had KMT2Ar, 12 patients (36%) had mNPM1, and five patients (15%) had NUP98r. Patients had received a median of three (range: 1-5) prior lines of therapy; 58% had prior venetoclax, 36% had prior hematopoietic stem cell transplantation (HSCT), and 6% had received a prior menin inhibitor.

The all-oral combination resulted in high rates of remission in patients with KMT2Ar, mNPM1, and NUP98r with an overall response rate (ORR)[1] of 82% (27/33) and a CR/CRh rate of 48% (16/33). In patients with minimal residual disease (MRD) status available, 65% (17/26) who achieved a response were MRD negative, and among patients who achieved a CR/CRh response, 88% (14/16) were MRD negative. 39% (13/33) of patients proceeded to HSCT following this combination, with 54% (7/13) of patients resuming revumenib post-HSCT.

With a median follow-up of 9.3 months (N=33), the 6-month overall survival (OS) was 68% (95% CI: 47%, 80%); median OS was not reached. The median duration of CR/CRh response was also not reached.

The combination was generally well tolerated in this population. The most common (>20%) Grade 3 or higher treatment-emergent adverse events (TEAEs) were febrile neutropenia (33%) and lung infection (33%). Grade 3 treatment-emergent differentiation syndrome (DS) was observed in one patient (3%), with no Grade 4 or Grade 5 events. Grade 3 treatment-emergent QTc prolongation was observed in two patients (6%) and Grade 4 was observed in one patient (3%) with no Grade 5 events.

"The latest SAVE data show high efficacy and the ability to combine revumenib with venetoclax and hypomethylating agents, which highlights the potential for this combination to become a treatment for patients with acute leukemias that are susceptible to menin inhibition," said Ghayas C. Issa, M.D., Associate Professor of Leukemia at The University of Texas MD Anderson Cancer Center. "In particular, the high rates of overall response, MRD negativity, and HSCT in the R/R cohort are very encouraging, as well as the initial duration of response and overall survival data. These promising data underpin our excitement to expand the SAVE trial to evaluate the combination in newly diagnosed AML patients who are older or unfit for intensive chemotherapy."

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

A larger data set with longer follow-up data (DCO: February 2024) from the pivotal Phase 2 portion of the AUGMENT-101 trial of revumenib in R/R KMT2A-rearranged (KMT2Ar) acute leukemia were presented at the 66th ASH Annual Meeting. This larger efficacy population is comprised of 97 patients, including the 57 patients from the previously reported Phase 2 protocol-defined interim efficacy analysis (DCO: July 2023).

As described in the previously announced ASH abstract, the CR+CRh rate was 23% (22/97), CRc was 42% (41/97), and ORR was 64% (62/97) among the 97 efficacy evaluable patients. In patients with 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 HSCT and nine resumed revumenib

post-HSCT.

During the oral session at the ASH meeting, the Company presented additional data from this larger data set showing that responses were observed across all major subgroups, including heavily pretreated patients, patients with prior venetoclax exposure, and patients of all ages. The updated analyses also show that of the 21 responders who proceeded to HSCT, 67% (14/21) went to transplant in CRc [38% (8/21) in CR/CRh and 29% (6/21) in CRp/CRi] and 33% (7/21) went to transplant in MLFS. Of the patients who proceeded to transplant in CRc and had MRD results available, 82% (9/11) were MRD negative.

Time to response was rapid with a median time to ORR of 1.0 months (range: 0.9-3.1) and median time to CR/CRh of 2.0 months (range: 0.9-4.6). As previously reported, the median duration of CR/CRh was 6.4 months among the 22 CR/CRh responders. Of note, with seven months of additional follow-up, the median duration of CR/CRh extended to 13 months among the 13 CR/CRh responders included in the interim analysis presented at the ASH Annual Meeting in 2023.

In this larger data set, which includes 116 patients in the safety population, revumenib was generally well tolerated and the safety profile was consistent with the Company's previously reported data. Treatment-related adverse events (TRAEs) and treatment-emergent adverse events (TEAEs) leading to treatment discontinuation were low at 5% (6/116) and 14% (16/116), respectively. The most common Grade 3 or higher TEAEs were consistent with previously reported data. Grade 3 treatment-emergent 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. No patients discontinued treatment due to differentiation syndrome, QTc prolongation, or cytopenias.

Initial Results from INTERCEPT Platform 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 AML may be an effective approach to maintaining patients in first or second remission.

As of the latest data cutoff, 14 patients with MRD relapse (13 with mNPM1 and one with KMT2Ar) were enrolled in the safety cohort and received revumenib. The median age was 56 years; 12 were in first remission and two were in second remission. Prior to starting revumenib treatment, two patients received venetoclax-based treatment and 12 received prior intensive chemotherapy-based treatment as their frontline therapy. In the safety cohort (N=14), the most common (>10%) Grade 3 or higher TEAEs were neutropenia, thrombocytopenia, and QTc interval prolongation. There were no reports of DS, and no Grade 5 events.

Among the 11 efficacy evaluable mNPM1 patients who received revumenib, 54% (6/11) patients had MRD reduction at any time, including 36% (4/11) who achieved MRD negativity. These initial data support the further evaluation of revumenib as a novel approach to targeting MRD relapse.

Copies of the ASH presentations are available in the Publications and Meeting Presentations section of Syndax's website.

Syndax Corporate Event

Data presented by the Company at the 66th ASH Annual Meeting from 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 KMT2A-Rearranged Acute Leukemia

Rearrangements of the KMT2A gene (KMT2Ar) give rise to an aggressive form of acute leukemia that is associated with a very poor prognosis and high relapse rates. It is estimated that more than 95% of patients with KMT2Ar acute leukemia have a KMT2A translocation, a type of rearrangement that occurs when part of one chromosome breaks and fuses to a different chromosome.

In KMT2Ar acute leukemias, binding of KMT2A fusion proteins with the protein called menin drives the activation of a leukemogenic transcriptional pathway. Inhibition of the menin-KMT2A interaction has been shown to alter the transcription of multiple genes including differentiation markers. KMT2Ar AML and ALL have a rapid onset and quick progression that makes early identification of a KMT2A rearrangement critical. It is routinely diagnosed through currently available cytogenetic or molecular diagnostic techniques.

About Mutant NPM1 (mNPM1) Acute Myeloid Leukemia (AML)

Mutations in the NPM1 gene are the most common genetic alteration in adult AML and are observed in approximately 30% of cases. Patients with relapsed or refractory mNPM1 AML have a poor prognosis and high unmet need. Similar to KMT2A-rearranged acute leukemia, mNPM1 AML is highly dependent on the expression of specific developmental genes shown to be negatively impacted by inhibitors of the menin-KMT2A interaction. mNPM1 AML is routinely diagnosed through currently available screening techniques. There are currently no approved targeted therapies for mNPM1 AML.

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

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