Syndax Presents Positive Data from Pivotal AUGMENT-101 Trial of Revumenib in Relapsed/Refractory KMT2Ar Acute Leukemia at Late-Breaking Oral Presentation During 65th ASH Annual Meeting

December 12, 2023

– Pivotal AUGMENT-101 trial met its primary endpoint at interim analysis of the pooled KMT2Ar AML and ALL cohorts (p-value = 0.0036); CR/CRh rate consistent across adult and pediatric patients –

– 63% overall response rate; responses observed across all major subgroups –

– Median overall survival at time of data cutoff of 8.0 months –

– Favorable safety and tolerability profile; treatment discontinuations were low at 6% with none due to differentiation syndrome or QTc prolongation –

– Supportive results from the AUGMENT-101 trial, including post-transplant maintenance data, continues to demonstrate consistent clinically meaningful responses across subgroups –

WALTHAM, Mass., Dec. 12, 2023 /PRNewswire/ -- Syndax Pharmaceuticals (Nasdaq: SNDX), a clinical stage biopharmaceutical company developing an innovative pipeline of cancer therapies, today presented positive data from the protocol-defined pooled analysis of the pivotal AUGMENT-101 trial of revumenib, a first-in-class menin inhibitor, in adult and pediatric patients with relapsed/refractory (R/R) KMT2A-rearranged (KMT2Ar) acute myeloid leukemia (AML) and acute lymphoid leukemia (ALL) at the 65th American Society of Hematology (ASH) Annual Meeting being held December 9-12, 2023 in San Diego, California. The pivotal results were featured in a late-breaking oral presentation titled "Revumenib Monotherapy in Patients with Relapsed/Refractory KMT2Ar Acute Leukemia: Topline Efficacy and Safety Results from the Pivotal AUGMENT-101 Phase 2 Study."

Additional supportive results from the AUGMENT-101 trial, including data from patients in the Phase 1 portion and patients who received revumenib maintenance therapy after hematopoietic stem cell transplant (HSCT), were also featured in two poster presentations at the meeting, titled "Revumenib Monotherapy in Patients with Relapsed/Refractory KMT2Ar Acute Leukemia: Efficacy and Safety Results from the AUGMENT-101 Phase 1/2 Study" and "Revumenib Maintenance Therapy Following Revumenib-Induced Remission and Transplant."

"We are thrilled to present additional detail on the positive results for revumenib in KMT2Ar acute leukemia that continue to demonstrate its consistently impressive clinical profile as a potential monotherapy for these patients," said Michael A. Metzger, Chief Executive Officer of Syndax. "We look forward to delivering on several important, near-term milestones across our pipeline, including submitting a New Drug Application to the U.S. Food and Drug Administration for revumenib for the treatment of R/R KMT2Ar acute leukemia at year-end."

Pivotal Phase 2 Portion of AUGMENT-101 Trial

The AUGMENT-101 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% confidence interval [CI]: [12.7, 35.8, one-sided p-value = 0.0036]) among the 57 efficacy evaluable patients in the pooled KMT2Ar acute leukemia population. The CR/CRh rate was 23% (10/44; 95% CI: 11.5, 37.8) in adult patients and 23% in pediatric patients (3/13; 95% CI: 5.0, 53.8), with a median time to CR/CRh of 1.9 months (95% CI: 0.9, 4.5). The CR/CRh responses in both the overall population and the AML subset were durable with a 6.4-month (95% CI: 3.4, NR) median duration as of the July 24, 2023 data cutoff, with 46% (6/13) remaining in response. Minimal residual disease (MRD) status was assessed in 10 of the 13 patients who achieved a CR/CRh, 70% (7/10) of whom were MRD negative. In patients who achieved a CRc (CR+CRh+CRp+Cri), 68% (15/22) achieved MRD negative status.

In the efficacy-evaluable patients, the overall response rate[1] was 63% (36/57; 95% CI: [49.3, 75.6]), and the composite response rate (CRc) was 44% (25/57). Minimal residual disease (MRD) status was assessed in 22 of the 25 patients who achieved a CRc, 68% (15/22) of whom were MRD negative. Responses were observed in all major subgroups, including across the number of prior treatments and prior stem cell transplant. A total of 14 (39%) patients who achieved an overall response underwent HSCT, eight of whom did not achieve a CR or CRh prior to transplant. Half (7/14) of the patients who had an HSCT received post-transplant maintenance with revumenib and three additional patients (3/14; 21%) were in follow-up and are eligible to restart revumenib as post-transplant maintenance. Median overall survival at the time of data cutoff was 8.0 months (95% CI: 4.1, 10.9).

"I am pleased that this pivotal dataset of revumenib as a monotherapy in heavily pretreated R/R patients continues to support its profile as a potential best- and first-in-class therapy," said Ibrahim Aldoss, M.D., Attending Physician and Associate Professor, Division of Leukemia, Department of Hematology & Hematopoietic Cell Transplantation at City of Hope, and Principal Investigator in the AUGMENT-101 trial. "Of particular note, the data presented today demonstrate rapid responses with revumenib, with a median time to CR/CRh of 1.9 months, which is particularly impressive in this patient population. Responses were also observed across all major subgroups, with a similar CR/CRh rate across adult and pediatric patients, which speaks to the wide clinical utility of revumenib across this underserved patient population."

AUGMENT-101 enrolled a total of 94 acute leukemia patients in the KMT2Ar cohorts of the pivotal trial as of the July 2023 data cutoff, 57 of whom had central confirmation of their KMT2Ar status, sufficient follow-up and were in the efficacy-evaluable population. The majority of patients included in the efficacy-evaluable population (56%; 32/57) relapsed following treatment with at least one salvage regimen (refractory relapse patients) prior to enrollment, including nearly half (46%; 26/57) having undergone prior stem cell transplant. Seventy-two percent (41/57) of patients were previously treated with venetoclax.

Revumenib was well tolerated and the safety profile was consistent with the Company's previously reported data. Treatment-related adverse events (TRAEs) leading to dose reductions and treatment discontinuation were low at 9% (8/94) and 6% (6/94), respectively. TRAEs of any grade in greater than 20% of patients included nausea (28%), differentiation syndrome (DS) (27%), and QTc prolongation (23%). Grade 3 DS was observed in 15% (14/94) of patients while one patient (1%) experienced Grade 4 DS and no patients experienced a Grade 5. Grade 3 QTc prolongation was observed in 14% (13/94) of patients, with no Grade 4 or 5 events. There were no discontinuations related to DS, cytopenias or QTc prolongation on the trial.

Revumenib Maintenance Therapy Post-HSCT

Data featured in a poster presentation from AUGMENT-101 Phase 1 patients who received revumenib maintenance therapy, including some ongoing for more than one year after HSCT, demonstrated revumenib duration of treatment in the maintenance setting at the time of this analysis ranged from 1 to 701 days, with treatment ongoing for nine of the 16 patients. CRc was maintained in 12 patients after HSCT and maintenance revumenib. MRD negative remissions were maintained in six patients as of the data cutoff with one patient converting from an MRD+ to MRD- response. Three patients remain on revumenib maintenance therapy for more than one-year post-transplant.

Phase 1 Portion of AUGMENT-101 Trial

In the Phase 1 portion of the study, patients were assigned to one of six dose-escalation cohorts designed to identify a recommended phase 2 dose (RP2D) for concomitant administration with a strong CYP3A4 inhibitor and without a strong CYP3A4 inhibitor. As of the July 2023 data cutoff, 77 patients with R/R KMT2Ar acute leukemia were enrolled in the Phase 1 study and were included in the overall population. Most patients were female (60%), and 34% of patients had ≥4 prior lines of therapy and 47% had prior HSCT.

Updated follow-up on Phase 1 data presented at the meeting continues to demonstrate clinically meaningful response, high percentage of responders proceeding to transplant, consistency of response across subgroups, and a manageable safety profile in heavily pretreated patients with R/R KMT2Ar acute leukemia. Phase 1 KMT2Ar patients demonstrated a CR/CRh rate of 31.2%, and ORR of 64.9%, with 38% proceeding to HSCT. In adults with AML (n=51), the CR/CRh rate was 37.3% and ORR was 68.6%, with 40% of responders proceeding to HSCT. Pediatric patients (n=15) demonstrated consistent response rates, with a CR/CRh rate of 20.0% and an ORR of 66.7%, with 40% of responders proceeding to transplant.

Copies of the ASH presentations are 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, also known as mixed lineage leukemia rearranged or MLLr, acute leukemias including ALL and AML, and NPM1-mutant AML. 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 BTD by the FDA for the treatment of adult and pediatric patients with R/R acute leukemia harboring a KMT2A rearrangement. Syndax expects to complete an NDA submission for KMT2Ar acute leukemia under the Oncology Center of Excellence Review RTOR Program by year-end 2023.

About AUGMENT-101

AUGMENT-101 is a Phase 1/2 open-label trial designed to evaluate the safety, tolerability, pharmacokinetics, and efficacy of orally administered revumenib. The Phase 1 dose escalation portion of AUGMENT-101 included two cohorts based on concomitant treatment with a strong CYP3A4 inhibitor. Arm A enrolled patients not receiving a strong CYP3A4 inhibitor, while Arm B enrolled patients receiving a strong CYP3A4 inhibitor. The Phase 2 pivotal portion of AUGMENT-101 has enrolled R/R patients across the following trial populations: patients with mNPM1 AML, patients with KMT2Ar AML, and patients with KMT2Ar ALL. Following the receipt of Breakthrough Therapy designation from the FDA for revumenib for the treatment of R/R acute leukemia harboring a KMT2A rearrangement, regardless of age or tumor type, and based on discussions with the FDA, the Company decided to pool data from the AUGMENT-101 cohorts enrolling R/R KMT2Ar AML and R/R KMT2Ar ALL. Based on the Independent Data Monitoring Committee (IDMC) recommendation at the protocol pre-specified interim analysis, the Company stopped the trial to further accrual in the KMT2A cohorts. The trial continues to enroll R/R patients with mNPM1 AML and expects to complete enrollment of this cohort in late 1Q24 or early 2Q24. The primary endpoint for each of the cohorts is efficacy as measured by complete remission rate (CR + CRh) per protocol, with secondary endpoints including duration of response (DOR) and overall survival (OS).

About KMT2A (MLL) Rearranged Acute Leukemia

Rearrangements of the KMT2A (mixed lineage leukemia or MLL) gene give rise to KMT2Ar acute leukemia that is known to have a poor prognosis. KMT2A genes produce fusion proteins that require interaction with the protein called menin to drive leukemic cancer growth. Disruption of the menin-KMT2Ar interaction has been shown to halt the growth of KMT2Ar leukemic cells. KMT2Ar acute leukemia can phenotypically appear as AML, ALL, or mixed phenotype acute leukemia (MPAL) and is routinely diagnosed through currently available cytogenetic or molecular diagnostic techniques. The median overall survival (OS) after standard of care first-line treatment, including intensive chemotherapy and transplant, is less than one year and the majority of patients suffer relapse within five years. With third line treatment or beyond, less than 5% of patients achieve complete remission (CR), and the median OS is less than three months. There are currently no approved therapies indicated for KMT2A-rearranged acute leukemia.

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 inhibitor of the menin–KMT2A binding interaction, and axatilimab, a monoclonal antibody that blocks the colony stimulating factor 1 (CSF-1) receptor. For more information, please visit www.syndax.com or follow the Company on 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 "may," "will," "expect," "plan," "anticipate," "estimate," "intend," "could," "believe" and similar expressions such as "look forward" (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 potential submission of an NDA by year-end, 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

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