# Syndax Announces Positive Data for Revumenib in Patients with Acute Leukemias from the BEAT AML, SAVE AML and AUGMENT-102 Phase 1 Combination Trials

December 11, 2023

*- Data collectively highlight revumenib's combination potential with current standard of care agents and support advancement into pivotal combination trials in the frontline setting -*

*- 100% CRc observed in BEAT AML trial exploring revumenib in combination with venetoclax/azacitidine in newly diagnosed mNPM1 or KMT2Ar AML -*

*-78% CRc observed in SAVE AML trial, an all-oral combination of revumenib, venetoclax and decitabine/cedazuridine in R/R mNPM1, NUP98r and KMT2Ar AML; five of nine patients continue in remission, 2 beyond 11 months at the time of the data cut -*

*- 33% CRc observed in AUGMENT-102 trial of revumenib in combination with fludarabine-cytarabine in pediatric R/R mNPM1, NUP98r and KMT2Ar AML -*

*- Revumenib was well tolerated with no new safety signals identified beyond those observed with the respective SOC combinations -*

WALTHAM, Mass., Dec. 11, 2023 /PRNewswire/ -- Syndax Pharmaceuticals (Nasdaq: SNDX), a clinical stage biopharmaceutical company developing an innovative pipeline of cancer therapies, today announced data from multiple trials of revumenib in combination with standard of care agents in patients with nucleophosmin mutant (mNPM1) and KMT2A-rearranged (KMT2r) relapsed/refractory (R/R) acute leukemias. Revumenib is the Company's highly selective, oral menin inhibitor.

Data to date demonstrate that revumenib has been well tolerated and demonstrated clinical activity in combination with venetoclax/hypomethylating agents in both the frontline and R/R acute myeloid leukemia (AML) settings, as well as in combination with fludarabine/cytarabine (FLA) chemotherapy in a heavily pretreated R/R pediatric AML population, including in patients who relapsed on FLA. In all three trials, patients are now receiving the full monotherapy recommended Phase 2 dose in combination with the standard of care agents. The new combination data collectively highlight revumenib's potential to safely combine with current standard of care agents across the acute leukemia treatment landscape, and support expansion of ongoing trials and advancement into additional combination trials currently in planning.

"Given the urgent need for novel, effective solutions for acute leukemia patients, we're excited to show clinical data demonstrating tolerability and compelling clinical responses when revumenib is added to current treatment regimens," said Michael A. Metzger, Chief Executive Officer. "The potential to safely combine with standard of care positions revumenib to become a cornerstone of treatment across a range of acute leukemia populations. In addition, current response rates seen across all three trials strengthen revumenib's already robust clinical profile as a monotherapy and furthers our conviction that revumenib could be a first- and best-in-class treatment for both KMT2Ar and mNPM1 acute leukemias."

**SAVE AML Trial**

Results from the SAVE AML trial of revumenib in combination with venetoclax-decitabine/cedazuridine in R/R AML were featured during an oral session at the 65$^{th}$ American Society of Hematology (ASH) Annual Meeting. The dose escalation phase of the trial tested revumenib at doses of 113 mg and 163 mg every 12 hours (q12h) in combination with azole antifungals known to strongly inhibit CYP3A4 enzymes. As of a data cutoff date of November 1, 2023, nine patients with KMT2Ar, mNPM1 or NUP98r AML or mixed phenotypic acute leukemia (MPAL) were enrolled and response evaluable at the time of the data cut. Patients received a median of three prior lines of therapy, including 56% who received prior venetoclax and 67% who received prior hypomethylating agents (HMA) or underwent prior stem cell transplant or both.

All nine patients attained a morphologic remission for an overall response rate of 100%, 78% of whom achieved a CRc[1] including 44% who achieved a CR/CRh. 67% (6/9) of patients in the trial attained minimal residual disease (MRD) negative status. Five patients transitioned to hematopoietic stem-cell transplantation (HSCT) following response. Two patients initiated post-transplant maintenance with revumenib and continue in remission for over 11 months.

The combination was well tolerated in this relapsed and refractory population, with no new safety signals observed beyond those reported for venetoclax-HMA. Grade ≥3 treatment related adverse events (TRAEs) included febrile neutropenia (56%), decreased platelets count (22%), decreased neutrophil count (22%) and lung infection (22%). There was one dose-limiting toxicity (DLT) at each dose level, Grade 4 thrombocytopenia that resolved after a dosing hold. There were no deaths due to TRAEs and no Grade 3 or higher QTc prolongation occurred.

**BEAT AML Trial**

The Company also announced data from the BEAT AML trial of revumenib in combination with venetoclax/azacitidine in newly diagnosed mNPM1 or KMT2Ar AML patients. The dose escalation phase of the trial tested revumenib at doses of 113 mg and 163 mg q12h in combination with azole antifungals known to strongly inhibit CYP3A4 enzymes. As of the data cutoff date of December 1, 2023, 13 newly diagnosed mNPM1 (n=8) or KMT2Ar (n=5) AML patients were efficacy evaluable. In the efficacy evaluable population, the CRc was 100% (13/13) after 1 – 2 cycles of induction. Eleven (85%) of 13 patients attained a CR/CRh and 92% (12/13) attained MRD negative status. Two patients proceeded to transplant.

No new safety signals were identified when revumenib was added to the standard venetoclax/azacitidine doublet in newly diagnosed AML patients. One patient at the lowest dose level, 113 mg q12h, experienced a DLT of decreased platelet counts; no DLTs were observed in the 163 mg q12h dose cohort. 31% of patients experienced differentiation syndrome or QTc prolongation, each included one (8%) Grade 3 event. All were managed without dose reductions. Cytopenias were manageable across the treatment experience with continuous dosing of venetoclax and revumenib. There were no increased safety issues outside of known adverse events reported for venetoclax/azacitidine toxicities.

An expansion cohort is planned to further evaluate safety and activity of this combination, and the full BEAT AML data will be presented at a future medical conference.

**AUGMENT-102 Trial**

The Company announced data from the AUGMENT-102 trial of revumenib in combination with fludarabine/cytarabine in a predominantly pediatric relapsed/refractory mNPM1 (n=1), NUP98r (n=1) and KMT2Ar (n=13) AML population. The dose-escalation phase of the trial tested revumenib at doses of 113 mg and 163 mg every 12 hours in combination with azole antifungals known to strongly inhibit CYP3A4 enzymes. As of the data cutoff date of September 20, 2023, 15 AML patients were efficacy evaluable, including three patients treated at 113 mg q12h and 12 patients treated at 163 mg q12h. The 163 mg q12hr cohort was comprised of primarily pediatric patients (median age of four), who had received a median of four prior lines of therapy. Across both dose groups, 50% of patients had failed prior treatment with fludarabine/cytarabine. Among the 12 patients treated at 163 mg q12h, four (33%) patients achieved a CRc including three (25%) patients that achieved a CR; four (33%) proceeded to transplant, including one mNPM1 patient who received a five-day course of decitabine prior to transplant.

The triplet of revumenib-fludarabine-cytarabine had an adverse event profile consistent with that observed with fludarabine-cytarabine alone, and no new safety signals were identified in the trial. Grade ≥3 TRAEs in over 30% of patients included decreased platelets (53%), decreased white blood cells (40%) and anemia (33%).

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

**Syndax Corporate Event**

The above combination data, along with other data presented through today at the 65th ASH Annual Meeting being held in San Diego, CA for both the revumenib and axatilimab clinical programs, will be highlighted at the Company's investor event on Monday, December 11, 2023 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 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 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 NPM1-Mutant Acute Myeloid Leukemia**

NPM1-mutant AML, which is distinguished by mutations in the NPM1 gene that drive the leukemic phenotype, is the most common type of cytogenetically normal adult AML and represents approximately 30% of all adult AML cases. This subtype of AML has a five-year overall survival rate of approximately 50%. Similar to KMT2A- rearranged acute leukemia, NPM1-mutant AML is highly dependent on the expression of specific developmental genes shown to be negatively impacted by inhibitors of the menin-KMT2A interaction. NPM1-mutant AML is routinely diagnosed through currently available screening techniques. There are currently no approved therapies indicated for NPM1-mutant AML.

**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," "conviction," "believe" 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 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 (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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View original content:https://www.prnewswire.com/news-releases/syndax-announces-positive-data-for-revumenib-in-patients-with-acute-leukemias-from-the-beat-aml-save-aml-and-augment-102-phase-1-combination-trials-302011153.html

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