Syndax to Initiate NDA Submission of Revumenib in Relapsed/Refractory KMT2Ar Acute Leukemia Under FDA's Real-Time Oncology Review Program

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– Solidifies first-to-market potential for revumenib –

– High unmet need in relapsed or refractory KMT2Ar patients in the U.S. provides a strong foundation for revumenib commercial launch –

WALTHAM, Mass., Oct. 24, 2023 /PRNewswire/ -- Syndax Pharmaceuticals (Nasdaq: SNDX), a clinical-stage biopharmaceutical company developing an innovative pipeline of cancer therapies, today announced that the Company will submit a New Drug Application (NDA) for revumenib in relapsed or refractory (R/R) KMT2Ar acute leukemia, including acute myeloid leukemia (AML) and acute lymphoid leukemia (ALL), under the U.S. Food and Drug Administration (FDA) Real-Time Oncology Review (RTOR) program. Revumenib is the Company's highly selective oral menin inhibitor.

During the Company's pre-NDA meeting, the FDA indicated that it would review the revumenib NDA submission for adult and pediatric KMT2Ar acute leukemia under the Oncology Center of Excellence RTOR Program. Inclusion in the RTOR program follows the previously announced FDA Breakthrough Therapy Designation (BTD) for the same indication and recent positive topline data from the AUGMENT-101 pivotal trial in R/R KMT2Ar acute leukemia. Syndax plans to initiate the NDA submission imminently and expects to complete the submission by year-end 2023.

"On the heels of announcing positive pivotal data earlier this month, we are delighted the FDA has agreed to review the application under the RTOR program, underscoring the urgent unmet need and the substantial improvement over available therapies that revumenib may offer to this underserved patient population," said Michael A. Metzger, Chief Executive Officer of Syndax. "Working with the FDA, we designed an innovative strategy to bring revumenib to the broadest population of KMT2Ar patients – adults and pediatrics, AML and ALL – as rapidly as possible. Syndax is in an excellent position to launch revumenib and axatilimab, two first- and best-in-class agents, in 2024 and deliver on multiple key milestones."

"Relapsed or refractory KMT2Ar acute leukemia patients have a particularly poor prognosis, and no drugs are approved for this difficult to treat disease," said Eytan M. Stein, M.D., Chief, Program for Drug Development in Leukemia, Department of Medicine at Memorial Sloan Kettering Cancer Center and Principal Investigator in the AUGMENT-101 trial. "Revumenib's clinical profile allowed 25% of the patients in the pivotal AUGMENT-101 trial to proceed to potentially curative transplant, which compares very favorably to the historical rate of <5% in this population.[1] Based on these results, long-term post-transplant maintenance is now potentially an option which represents an important paradigm shift for how physicians treat patients with KMT2Ar R/R acute leukemias."

Data from the AUGMENT-101 pivotal trial in R/R KMT2Ar acute leukemia will serve as the basis for the NDA submission under the RTOR program. AUGMENT-101 is a Phase 1/2 open-label trial designed to evaluate the safety, tolerability, pharmacokinetics and efficacy of revumenib as a monotherapy. As previously reported, the AUGMENT-101 R/R KMT2Ar cohort was stopped early for efficacy following a protocol-defined interim analysis based on achieving its primary endpoint of complete remission (CR) or a CR with partial hematological recovery (CRh) rate. These results demonstrated that revumenib monotherapy provided significant clinical benefit including deep, durable molecular remissions with a high proportion of patients proceeding to potentially curative transplant and re-starting revumenib therapy as maintenance. Revumenib was well tolerated, consistent with the Company's earlier data.

About RTOR

RTOR provides a more efficient review process for oncology drugs to ensure that safe and effective treatments are available to patients as early as possible, while improving review quality and engaging in early iterative communication with the applicant. Specifically, it allows for close engagement between the sponsor and the FDA throughout the submission process and it enables the FDA to review individual sections of modules of a drug application rather than requiring the submission of complete modules or a complete application prior to initiating review.[2] From the start of the program in 2018, 22 original applications (including sNDAs and NDAs) have been reviewed under the RTOR Program, resulting in 19 U.S. drug approvals while 3 are still being reviewed. Additional information about RTOR can be found at: https://www.fda.gov/about-fda/oncology-center-excellence/real-time-oncology-review-pilot-program

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 plans to initiate the NDA submission for KMT2Ar acute leukemia under the Oncology Center of Excellence Review RTOR Program imminently and expects to complete the submission by year-end 2023.

About the AUGMENT-101 trial

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 NPM1-mutant 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 is stopping 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 by year-end. 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, with less than 25% of adult patients surviving past five years. 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. Most R/R patients treated with second-line therapy relapse within the first year. With third line treatment or beyond, only a small percentage 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," "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 as well as the potential impact of RTOR on the Company's submission timeline, and the potential use of our product candidates to treat various cancer indications. 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] Issa GC et al. Blood Cancer J. 2021 Sept 29;11(9);162

[2] Gao YG, Roberts S, Guy A. Maximizing Regulatory Review Efficiency: The Evolution of the FDA OCE RTOR Pilot. Ther Innov Regul Sci. 2022 Mar;56(2):212-219.

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