September 29, 2021

Syros Announces First Patient in Dose Confirmation Study of SY-2101, a Novel Oral Form of Arsenic Trioxide, in Acute Promyelocytic Leukemia

Confirmatory Dose and PK Data Expected in First Half of 2022, with a Phase 3 Trial Expected to Begin in 2022

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Syros Pharmaceuticals (NASDAQ:SYRS), a leader in the development of medicines that control the expression of genes, today announced that the first patient has been dosed in the dose confirmation study of SY-2101, a novel oral form of arsenic trioxide (ATO). The trial will evaluate the pharmacokinetics (PK), safety, and tolerability of SY-2101 to confirm the optimal dose to advance into a planned Phase 3 clinical trial in newly diagnosed acute promyelocytic leukemia (APL) patients.

“The current standard of care cures most patients but is tremendously burdensome, requiring regular and lengthy infusions of an IV formulation of ATO over nearly a yearlong course of treatment,” said Farhad Ravandi, M.D., Professor of Medicine, Chief of Section of Acute Myeloid Leukemia, Department of Leukemia at The University of Texas – MD Anderson Cancer Center. “An oral form of ATO that offers similar efficacy while dramatically reducing the treatment burden would represent a major advance for APL patients. The preliminary Phase 1 data for SY-2101 are very promising, and I look forward to its continued advancement in the current and future studies.”

APL is a well-defined subtype of acute myeloid leukemia (AML), which accounts for about 10% of AML cases, with approximately 2,000 APL patients diagnosed annually in the United States and Europe. An intravenously administered formulation of ATO is approved for use in combination with All-Trans-Retinoic-Acid (ATRA) in newly diagnosed APL and, while curative in more than 80% of patients, its administration requires up to 140 infusions over the typical 10-month course of induction and consolidation treatment. In an earlier Phase 1 clinical trial, SY-2101, which is dosed once daily, demonstrated oral bioavailability, PK exposures similar to IV ATO, and a generally well-tolerated safety profile.

"We are thrilled to now be dosing patients in our dose confirmation study of SY-2101,” said David A. Roth, M.D., Chief Medical Officer at Syros. “This milestone represents an important step toward delivering a new option for people with APL and a meaningful advance in our efforts to build a leading portfolio of targeted hematology therapies. We believe SY-2101 could quickly become the new standard of care for APL by offering patients similar efficacy with a substantially more accessible and convenient therapy. We plan to move swiftly from our dose confirmation study into a Phase 3 trial next year, with the goal of filing a New Drug Application (NDA) in 2024.”

The dose confirmation study is expected to enroll up to 24 patients with newly diagnosed APL and will evaluate safety, tolerability, and PK as well as the effect of food on the absorption of SY-2101. Patients will be enrolled during the consolidation phase of their APL treatment and will receive single doses of SY-2101 in a fasted state, SY-2101 in a fed state, and IV ATO. Patients will then have the option to roll over into a multiple-dose cohort to receive either SY-2101 or IV ATO, which will provide additional data on the steady state PK and safety of SY-2101 in comparison to IV ATO. Syros expects to report data from this study in the first half of 2022.

Based on the results of the dose confirmation study, Syros expects to initiate a Phase 3 clinical trial in newly diagnosed APL patients. Based on input from the FDA, Syros believes molecular complete response rate and event-free survival in comparison to historical control data with IV ATO may support accelerated and full approval, respectively.

About Syros Pharmaceuticals
Syros is redefining the power of small molecules to control the expression of genes. Based on its unique ability to elucidate regulatory regions of the genome, Syros aims to develop medicines that provide a profound benefit for patients with diseases that have eluded other genomics-based approaches. Syros is advancing a robust clinical-stage pipeline, including: tamibarotene, a first-in-class oral selective RARα agonist in RARA-positive patients with higher-risk myelodysplastic syndrome and acute myeloid leukemia; SY-2101, a novel oral form of arsenic trioxide in patients with acute promyelocytic leukemia; and SY-5609, a highly selective and potent oral CDK7 inhibitor in patients with select solid tumors and blood cancers. Syros also has multiple preclinical and discovery programs in oncology and monogenic diseases. For more information, visit www.syros.com and follow us on Twitter (@SyrosPharma) and LinkedIn.

Cautionary Note Regarding Forward-Looking Statements
This press release contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995, including without limitation statements regarding Syros's clinical development plans with respect to SY-2101, the timing of anticipated data readouts from the dose confirmation study of SY-2101, the anticipated timing for initiating a Phase 3 trial of SY-2101, the potential submission of a new drug application and the likelihood of regulatory approval, the and the ability of SY-2101 to have a benefit for patients. The words ‘‘anticipate,’’ ‘‘believe,’’ ‘‘continue,’’ ‘‘could,’’ ‘‘estimate,’’ ‘‘expect,’’ “hope,” ‘‘intend,’’ ‘‘may,’’ ‘‘plan,’’ ‘‘potential,’’ ‘‘predict,’’ ‘‘project,’’ ‘‘target,’’ ‘‘should,’’ ‘‘would,’’ and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward-looking statements as a result of various important factors, including Syros' ability to: advance the development of SY-2101 under the timelines it projects in current and future clinical trials; demonstrate in any current and future clinical trials the requisite safety, efficacy and combinability of SY-2101; sustain the responses seen to date with SY-2101; obtain and maintain patent protection for its drug candidates and the freedom to operate under third party intellectual property; obtain and maintain necessary regulatory approvals; identify, enter into and maintain collaboration agreements with third parties; manage competition; manage expenses; raise the substantial additional capital needed to achieve its business objectives; attract and retain qualified personnel; and successfully execute on its business strategies; risks described under the caption “Risk Factors” in Syros' Annual Report on Form

10-K for the year ended December 31, 2020 and Quarterly Report on Form 10-Q for the quarter ended June 30, 2021, each of which is on file with the Securities and Exchange Commission; and risks described in other filings that Syros makes with the Securities and Exchange Commission in the future. In addition, the extent to which the COVID-19 pandemic continues to impact Syros' workforce and its clinical trial operations activities, and the operations of the third parties on which Syros relies, will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the duration and severity of the pandemic, additional or modified government actions, and the actions that may be required to contain the virus or treat its impact. Any forward-looking statements contained in this press release speak only as of the date hereof, and Syros expressly disclaims any obligation to update any forward-looking statements, whether because of new information, future events or otherwise.

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