



Syros Announces New Data from Phase 2 Trial of SY-1425 in Combination with Azacitidine Demonstrating High Response Rates, Rapid Onset of Action and Favorable Tolerability Profile in RARA-Positive Newly Diagnosed Unfit AML Patients

62% Composite Complete Response Rate, with 82% of Patients Achieving or Maintaining Transfusion Independence

Data Support RARA as the Optimal Predictive Biomarker for Patient Selection

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Syros Pharmaceuticals (NASDAQ: SYRS), a leader in the development of medicines that control the expression of genes, today announced that updated clinical data from its ongoing Phase 2 trial evaluating SY-1425, its first-in-class selective retinoic acid receptor alpha (RAR α) agonist, in combination with azacitidine, continue to demonstrate high complete response rates, rapid onset of action and a favorable tolerability profile in a genomically defined subset of newly diagnosed acute myeloid leukemia (AML) patients who are not suitable candidates for standard intensive chemotherapy. These data are being presented at the European School of Haematology (ESH) 5th International Conference Acute Myeloid Leukemia "Molecular and Translational": Advances in Biology and Treatment in Estoril, Portugal.

"I am very encouraged by these data. AML patients continue to need new treatment options, despite recent advances in the field, that are well-tolerated and can be used in combination to extend survival and improve quality of life," said Stéphane de Botton, M.D., Head of Acute Myeloid Malignancies at Institut Gustave Roussy and a clinical investigator in the Phase 2 trial of SY-1425. "These data show that SY-1425, a targeted therapy, in combination with azacitidine is highly active in a subset of patients that can be readily identified and that the combination is generally well-tolerated even in very sick AML patients. I believe SY-1425 is a promising combination agent with the potential to provide a meaningful benefit for a subset of AML patients, and I look forward to its continued development."

"These data mark an important milestone in the development of SY-1425," said David A. Roth, M.D., Chief Medical Officer of Syros. "SY-1425 in combination with azacitidine continues to demonstrate high complete response rates, rapid onset of action and a favorable tolerability profile in RARA-positive AML patients. As we study the combination in more patients, we are also seeing a high rate of transfusion independence and early evidence of durable responses. We are gratified to see our discovery of this novel patient subset, as defined by our RARA biomarker, translating into clinical benefit. These results demonstrate the power of our gene control platform to identify which genes to modulate in which patients to maximize the chances of providing them with a profound benefit. We look forward to continuing to evaluate SY-1425 in our ongoing study and to reporting potential proof-of-concept data next year in RARA-positive relapsed or refractory AML patients."

Updated Clinical Data on SY-1425 in Combination with Azacitidine in Newly Diagnosed, Unfit AML Patients

Syros presented updated data from its Phase 2 trial of SY-1425 in combination with azacitidine, a standard-of-care hypomethylating agent, in newly diagnosed unfit AML patients. The trial evaluated the safety and efficacy of the combination in patients with either the RARA or IRF8 biomarker, as well as in patients without the biomarkers. All patients were treated with azacitidine administered at standard daily doses of 75 mg/m² intravenously or subcutaneously for seven days, followed by SY-1425 administered at 6 mg/m²/day orally, divided in two doses, for the remainder of each 28-day cycle.

As of Aug. 22, 2019, 40 newly diagnosed unfit AML patients had been enrolled in the trial and were eligible for the safety analysis. The median age of patients enrolled in the study was 76. Of the 17 biomarker-positive patients evaluable for response, 13 were RARA-positive and four were IRF8-positive. Enrollment in the newly diagnosed unfit cohorts of the ongoing Phase 2 trial is nearly complete. Syros will continue to follow patients enrolled in the trial to further characterize the overall profile of the combination, including safety, efficacy and durability of response.

Clinical Activity Data

- 62% complete response (CR) and complete response with incomplete blood count recovery (CRi) rate, as defined by Revised International Working Group, IWG, criteria), in RARA-positive patients.
- 54% CR rate in RARA-positive patients, consisting of seven CRs, including three molecular CRs and three cytogenetic CRs.
- Most initial responses were seen at the first response assessment.
- Duration of these responses in RARA-positive patients was up to 344 days, with three of the eight responding patients having responses lasting beyond seven months at the time of the data cutoff.
- 82% of RARA-positive patients achieved or maintained transfusion independence.
- Responses were seen in RARA-positive patients across AML risk groups, including patients with mutations that are typically associated with poor outcomes.
- In patients with only the IRF8-biomarker, the CR/CRi rate was 0%, supporting Syros' decision to use RARA as the sole biomarker for patient selection in SY-1425 clinical trials going forward. Based on data from 112 newly diagnosed patients screened for its clinical trial, Syros believes that approximately 30% of newly diagnosed AML patients are RARA-positive.
- In the 22 response-evaluable RARA-negative patients, the CR/CRi rate was 27%, which is consistent with the published response rates of 18-29% observed in newly diagnosed unfit AML patients treated with single-agent azacitidine.

Safety Data

- SY-1425 in combination with azacitidine was generally well-tolerated with no evidence of increased toxicities beyond what is seen with either SY-1425 or azacitidine alone.
- Rates of myelosuppression, including neutropenia, were comparable to reports of single-agent azacitidine in this AML population.
- The majority of non-hematologic AEs were low grade.
- Across all grades and of all causalities, the most commonly reported AEs were nausea (38%), decreased appetite (38%), constipation (33%), fatigue (33%) and peripheral edema (30%).
- The most commonly reported Grade 3 or higher AEs (all causality) were thrombocytopenia (25%), anemia (23%), and febrile neutropenia (23%).

The poster presented at ESH is now available on the Publications and Abstracts section of the Syros website at www.syros.com.

The ongoing Phase 2 trial is actively enrolling patients with relapsed or refractory AML patients who are positive for the RARA biomarker. Syros expects to report potential proof-of-concept from the cohort in relapsed or refractory AML patients in 2020. Additional details about the Phase 2 trial of SY-1425 can be found using the identifier NCT02807558 at www.clinicaltrials.gov.

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. Currently focused on cancer and monogenic diseases, Syros is advancing a robust pipeline of development candidates, including SY-1425, a first-in-class oral selective RAR α agonist in a Phase 2 trial in a genomically defined subset of acute myeloid leukemia patients, and SY-5609, a highly selective and potent oral CDK7 inhibitor in investigational new drug application-enabling studies in cancer. Syros also has multiple preclinical and discovery programs in oncology and sickle cell disease. 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 the promise of SY-1425 as a combination

agent and the ability of SY-1425 to provide a meaningful benefit to AML patients, the reporting of potential proof-of-concept data for SY-1425 in combination with azacitidine in relapsed or refractory AML patients in 2020, the predictive value of the RARA biomarker, and the power of Syros' gene control platform. 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 its programs, including SY-1425, under the timelines it projects; demonstrate in clinical trials the requisite safety, efficacy and combinability of SY-1425; sustain the response rates and durability of response seen to date with SY-1425 in combination with azacitidine; successfully develop a companion diagnostic test to identify patients with the RARA biomarker; obtain and maintain patent protection for SY-1425 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, 2018 and Quarterly Report on Form 10-Q for the quarter ended June 30, 2019, 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. 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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