December 8, 2019

Syros Presents on Identification of Novel Fetal Hemoglobin Repressor as Part of Broader Drug Discovery Program in Sickle Cell Disease at 61st Annual ASH Meeting

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Syros Pharmaceuticals (NASDAQ:SYRS), a leader in the development of medicines that control the expression of genes, today announced that it has discovered and validated a novel fetal hemoglobin repressor, Nuclear Factor I X (NFIX), using its gene control platform. The finding sheds light on how the gamma-globin gene, which leads to the production of fetal hemoglobin, is controlled and points to new potential targets for therapeutic intervention in sickle cell disease. These data will be presented in an oral presentation tomorrow at the 61st American Society of Hematology (ASH) Annual Meeting and were highlighted today in an ASH press briefing.

“This discovery highlights the power of our platform to elucidate regulatory regions of the genome to control the expression of a single gene for therapeutic benefit,” said Eric R. Olson, Ph.D., Syros’s Chief Scientific Officer. “Based on real-world genetic and clinical data from patients, we believe it is possible to provide a functional cure for sickle cell disease by switching on the gamma-globin gene, which is typically turned off at birth, to make healthy red blood cells. Our discovery of NFIX as a critical player in silencing the gamma-globin gene opens up new potential therapeutic approaches as we advance our effort to discover an oral medicine that addresses the root cause of disease in sickle cell patients.”

The focus of Syros’ drug discovery program in sickle cell disease is to develop an oral medicine to mimic a condition found in a subset of patients, who also inherit a hereditary persistence of fetal hemoglobin (HPFH) mutation, in which the gamma-globin gene remains activated after birth. Despite having the mutated adult beta-globin gene that causes sickled cells, these patients are largely asymptomatic because the activated gamma-globin gene leads to the production of enough fetal hemoglobin for red blood cells to function normally.

Using its gene control platform, Syros scientists analyzed and compared regulatory regions of the genome in red blood cell precursors, known as erythroblasts, at various stages of maturity from fetal and adult sources to identify novel drug targets involved in the switch from fetal to adult hemoglobin expression. The genome-wide analysis pointed to NFIX as a potential fetal hemoglobin repressor. The scientists then validated the role of NFIX in silencing fetal hemoglobin by knocking down the NFIX gene in primary cells and an erythroid cell line that expresses adult hemoglobin. The data showed:

- Increases in expression of gamma-globin mRNA comparable to known fetal hemoglobin repressors.
- Detectable levels of fetal hemoglobin in nearly 100% of cells, compared to 16% of cells when the NFIX gene was not knocked down.

- Increases in total fetal hemoglobin levels to 40%, exceeding levels that are associated with a functional cure in sickle cell patients with HPFH.

The oral presentation will take place tomorrow during the Thalassemia and Globin Gene Regulation: Hemoglobin Regulation and Beta Thalassemia Research session from 4:30-6:30 p.m. ET in Valencia A (W415A) at the Orange County Convention Center, Valencia A (W415A). The ASH presentation is also now available on the Publications and Abstracts section of the Syros website at www.syros.com.

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 pipeline of development candidates, including SY-1425, a first-in-class oral selective RARα 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 monogenic diseases, including 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 power of the Company's gene control platform and the Company's ability to discover an oral medicine that can restore healthy blood function in sickle cell patients and provide a functional cure for sickle cell disease. 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: successfully advance the development of its programs; demonstrate in any current and future clinical trials the requisite safety, efficacy and combinability of its drug candidates; replicate scientific and non-clinical data in clinical trials; 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, 2018 and Quarterly Report on Form 10-Q for the quarter ended September 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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