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Syros Announces Approval of Investigational Device Exemption (IDE) for Blood Test to Identify Cancer Patients with Proprietary Biomarkers

IDE Allows Syros to Expand Ongoing Phase 2 Clinical Trial of SY-1425 into Newly Diagnosed Acute Myeloid Leukemia and Low-Risk Myelodysplastic Syndrome Patients

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Syros Pharmaceuticals (NASDAQ: SYRS) today announced that the U.S. Food and Drug Administration (FDA) has approved an investigational device exemption (IDE) for a laboratory-based blood test to detect proprietary biomarkers discovered using the Company's gene control platform to select patients for enrollment in the ongoing Phase 2 clinical trial of Syros' lead drug candidate, SY-1425, a selective retinoic acid receptor alpha (RARα) agonist.

The approval of the IDE allows Syros to expand its Phase 2 clinical trial to include newly diagnosed acute myeloid leukemia (AML) patients 60 years of age or older who are not suitable candidates for standard chemotherapy and low-risk transfusion-dependent myelodysplastic syndrome (MDS) patients who test positive for the biomarkers. The trial is currently enrolling genomically defined patients with relapsed or refractory AML or high-risk MDS identified using the biomarker test.

"The approval of the IDE is an important milestone in the development of SY-1425 because it allows us to expand into a broader set of AML and MDS patients and potentially benefit four patient populations with high unmet medical need," said Nancy Simonian, M.D., Syros' Chief Executive Officer. "This achievement is a testament to our ability to discover genomically defined subsets of patients who are most likely to respond to our gene control therapies and collaborate with partners to develop biomarker tests to identify these patient subsets, which is a key part of our strategy to advance a new wave of gene control medicines."

Using its gene control platform, Syros discovered subsets of AML and MDS patients whose tumors have a highly specialized regulatory region of non-coding DNA, known as a super-enhancer, that is associated with the *RARA* gene, which codes for the RARα transcription factor. The super-enhancer is believed to lead to over-production of the RARα transcription factor, locking cells in an immature, undifferentiated and proliferative state. Syros further investigated this biology directly in patient tissues and conducted preclinical studies showing that the *RARA* super-enhancer is predictive of response to treatment with SY-1425 in models of AML. Based on those data, Syros developed a biomarker strategy for its Phase 2 trial to identify these subsets of AML and MDS patients it believes are most likely to respond to treatment with SY-1425. Syros estimates that approximately 25 percent of AML and MDS patients have the *RARA* super-enhancer.

The proprietary biomarkers were developed into a validated laboratory test in collaboration with a diagnostics company under Clinical Laboratory Improvement Amendment, or CLIA, guidelines using a well-established diagnostic platform. The test is currently being used to select relapsed or refractory AML or high-risk MDS patients in the ongoing Phase 2 trial of SY-1425. The diagnostics company submitted the IDE to the FDA, which was required for prospective selection of patients with newly diagnosed AML and low-risk transfusion-dependent MDS for the trial.

The Phase 2 clinical trial of SY-1425 is a multi-center, open-label trial exploring safety and efficacy. The primary endpoint is overall response rate for AML and high-risk MDS patients and red blood cell transfusion-independence rate for low-risk MDS patients. Other endpoints include assessment of pharmacodynamic biomarkers, duration of response, safety and tolerability, and overall and progression-free survival. Additional details about the trial can be found using the identifier NCT02807558 at www.clinicaltrials.gov.

About Syros Pharmaceuticals
Syros Pharmaceuticals is pioneering the understanding of the non-coding region of the genome to advance a new wave of medicines that control expression of disease-driving genes. Syros has built a proprietary platform to systematically and efficiently analyze this unexploited region of DNA in human disease tissue to identify and drug novel targets linked to genomically defined patient populations. Because gene expression is fundamental to the function of all cells, the Company's gene control platform has broad potential to achieve profound and durable benefit across a range of diseases. Syros is focused on cancer and immune-mediated diseases and is advancing a growing pipeline, including its lead drug candidates SY-1425, a selective RARα agonist for genomically defined subsets of patients identified by its platform, for a range of cancers including acute myeloid leukemia and myelodysplastic syndrome, and SY-1365, a selective CDK7 inhibitor for a range of blood cancers and solid tumors. Led by a team with deep experience in drug discovery, development and commercialization, Syros is located in Cambridge, Mass.

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 potential therapeutic benefit of treatment with SY-1425 in subsets of AML and MDS patients identified with the Company's biomarker; the Company's strategies, plans and goals for SY-1425, including the expansion of development into additional AML and MDS patient populations; the percentage of AML and MDS patients who have the *RARA* super-enhancer; and the potential benefits of the Company's gene control platform. The words ‘‘anticipate,’’ ‘‘believe,’’ ‘‘continue,’’ ‘‘could,’’ ‘‘estimate,’’ ‘‘expect,’’ ‘‘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 in current and future clinical trials; obtain and maintain patent protection for its drug candidates and the freedom to operate under third party intellectual property; 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; successfully develop a companion diagnostic test to

identify patients with biomarkers associated with the *RARA* super-enhancer; 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 the company’s Quarterly Report on Form 10-Q for the quarter ended June 30, 2016, which is on file with the Securities and Exchange Commission; and risks described in other filings that the company 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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