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Syros Announces FDA Acceptance of IND to Advance SY-1365, Its First-in-Class Selective CDK7 Inhibitor, into Phase 1 Clinical Trial in Patients with Advanced Solid Tumors

– Company on Track to Initiate Study in Second Quarter of 2017 –

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Syros Pharmaceuticals (NASDAQ: SYRS), a biopharmaceutical company pioneering the discovery and development of medicines to control the expression of disease-driving genes, announced today that the U.S. Food and Drug Administration (FDA) accepted the Company's Investigational New Drug (IND) application to advance SY-1365, its first-in-class selective cyclin-dependent kinase 7 (CDK7) inhibitor, into a Phase 1 clinical trial in patients with advanced solid tumor malignancies, including transcriptionally dependent cancers such as triple negative breast, small cell lung and ovarian cancers. Syros is on track to initiate the Phase 1 trial in the second quarter of 2017.

“We are delighted to reach this important milestone for patients and for Syros,” said Nancy Simonian, M.D., Chief Executive Officer of Syros. “SY-1365 represents a promising new approach for cancers that are dependent on high expression of oncogenic transcription factors for their growth and survival. By selectively targeting CDK7, SY-1365 has been shown to lower the expression of these disease-driving transcription factors, inducing substantial anti-tumor activity in multiple preclinical models. We are committed to developing SY-1365 as quickly and efficiently as possible for patients with transcriptionally dependent cancers who are in need of better treatment options and have designed the Phase 1 clinical trial to give us early demonstration of proof-of-mechanism.”

In this Phase 1 trial, Syros plans to enroll approximately 70 patients with advanced solid tumors, including an expansion cohort in triple negative breast, small cell lung and ovarian cancers at multiple sites the United States. The trial will test the safety and tolerability of escalating doses of SY-1365, with the goal of establishing a maximum tolerated dose and a recommended Phase 2 dose. Additional study objectives include assessing pharmacodynamic changes and early signs of biological activity using biomarkers and clinical efficacy as measured by response rate using radiographic measures. Syros plans to expand future clinical development of SY-1365 into acute leukemias based on the data generated in this trial.

SY-1365 has shown significant anti-proliferative and pro-apoptotic activity in multiple *in vitro* and *in vivo* models of difficult-to-treat solid tumors, including triple negative breast, small cell lung and ovarian cancers. SY-1365 has induced anti-tumor activity in both cell line-derived

xenograft and patient-derived xenograft models of triple negative breast cancer, including regressions at a twice weekly dosing regimen consistent with the initial regimen planned for the Phase 1 clinical trial. SY-1365 has also been shown to preferentially kill cancer cells over non-cancerous cells in preclinical models of transcriptionally dependent solid tumors and acute leukemias and can lower the expression of oncogenic transcription factors, including MYC.

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 that is designed 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, Syros' gene control platform has broad potential to create medicines that achieve profound and durable benefit across a range of diseases. Syros is currently focused on cancer and immune-mediated diseases and is advancing a growing pipeline of gene control medicines. Syros' lead drug candidates are SY-1425, a selective RARα agonist in a Phase 2 clinical trial for genomically defined subsets of patients with acute myeloid leukemia and myelodysplastic syndrome, and SY-1365, a selective CDK7 inhibitor with potential in a range of solid tumors and blood cancers. 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 initiation of the planned Phase 1 clinical trial of SY-1365, the ability of this trial to provide early evidence of proof-of-mechanism, the progression of clinical development of SY-1365 into expansion cohorts of solid tumor patients and acute leukemias, and the benefits of Syros' 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 Syros' Annual Report on Form 10-K for the year ended December 31, 2016, 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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