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Syros Announces First Patient Dosed in Phase 1 Clinical Trial of SY-1365, Its First-in-Class Selective CDK7 Inhibitor, in Patients with Advanced Solid Tumors

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 first patient has been dosed in the Phase 1 clinical trial of SY-1365, its first-in-class selective cyclin-dependent kinase 7 (CDK7) inhibitor, in patients with advanced solid tumors, including transcriptionally dependent cancers such as triple negative breast, small cell lung and ovarian cancers.

“SY-1365 represents a promising new approach for treating a number of aggressive cancers that have eluded treatment with other targeted approaches,” said Anthony W. Tolcher, M.D., Director of Clinical Research at South Texas Accelerated Research Therapeutics (START), and a clinical investigator in the trial. “Certain cancers are particularly dependent on high expression of transcription factors for their growth and survival, and SY-1365 has shown substantial anti-tumor activity in preclinical models of these cancers. We’re pleased to have enrolled the first patient in this clinical trial and look forward to further investigating SY-1365 for patients with these difficult-to-treat solid tumors.”

SY-1365 has shown significant anti-proliferative and pro-apoptotic activity in multiple preclinical 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 complete regressions at a twice weekly dosing regimen consistent with the initial regimen being used in the Phase 1 clinical trial. In preclinical models, SY-1365 has also been shown to preferentially kill cancer cells over non-cancerous cells and can lower the expression of oncogenic transcription factors, including MYC.

“Patients with triple negative breast, small cell lung and ovarian cancers, as well as other transcriptionally dependent cancers, are in dire need of better treatment options,” said David A. Roth, M.D., Chief Medical Officer of Syros. “Based on the strong preclinical data, we believe SY-1365 could provide a meaningful benefit for patients with these cancers. We have designed our Phase 1 trial to efficiently assess early proof of mechanism during the dose escalation phase and early anti-tumor activity by focusing the expansion phase of the trial on a set of transcriptionally dependent tumors that are most sensitive to CDK7 inhibition and for which early anti-tumor activity may be observed.”

The Phase 1 trial is a multi-center, open-label trial that is expected to enroll approximately 70 patients with advanced solid tumors, including expansion cohorts focused on

transcriptionally dependent cancers. The primary objective of the trial is to assess 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 and regimen. The dose-escalation phase will be open to solid tumor patients for whom standard curative or palliative measures do not exist or are no longer effective. Following the dose-escalation phase, expansion cohorts are planned to further evaluate the safety and anti-tumor activity of SY-1365 in patients with triple negative breast, small cell lung and ovarian cancers, to confirm a recommended Phase 2 dose and regimen, and to enroll patients with tumors of any histology in a cohort focused on analyzing biopsied tumor tissue. Syros plans to expand future clinical development of SY-1365 into acute leukemias based on the data generated in this trial. Additional details about the trial can be found using the identifier NCT03134638 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 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 RAR α 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 clinical utility of SY-1365, Syros' ability to advance and expand development of SY-1365, the ability of the Phase 1 clinical trial to show proof-of-mechanism, the number of patients to be enrolled in the Phase 1 clinical trial, 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-1365, 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 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, 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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