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New Publication in Cancer Research Highlights Discovery of SY-1365, a First-in-Class Selective CDK7 Inhibitor, and its Promise as a Potentially Transformative Targeted Approach for Difficult-to-Treat Cancers

SY-1365 Currently in Phase 1 Clinical Trial in Relapsed and Treatment-Resistant Ovarian and Breast Cancer Patients

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Syros Pharmaceuticals (NASDAQ: SYRS), a leader in the development of medicines that control the expression of genes, today announced the online publication of a new manuscript, *Discovery and Characterization of SY-1365, a Selective, Covalent Inhibitor of CDK7*, in the American Association for Cancer Research's (AACR) journal, *Cancer Research*. SY-1365, a first-in-class selective cyclin-dependent kinase 7 (CDK7) inhibitor, is currently being investigated in a Phase 1 clinical trial as a single agent and in combination with standard-of-care therapies in multiple ovarian and breast cancer patient populations that lack effective treatment options. This publication highlights the discovery, mechanism of action and promise of SY-1365 as a new targeted approach for a range of difficult-to-treat cancers.

"SY-1365 represents a potentially transformative targeted approach for a number of cancers that have eluded treatment with existing approaches," said Eric R. Olson, Ph.D., Syros' Chief Scientific Officer. "While CDK7 has long been a target of interest, it was historically difficult-to-drug. This new publication profiles our work in discovering SY-1365, which we believe to be the most advanced selective CDK7 inhibitor in clinical development, and the substantial anti-tumor activity seen in preclinical models that supported its advancement into the clinic. We are excited by the promise of CDK7 inhibition and the potential benefit SY-1365 may bring to patients who are in dire need of better therapies."

Syros is currently conducting a Phase 1 clinical trial assessing the safety and efficacy of SY-1365 as a single agent and in combination with standard-of-care therapies in multiple ovarian and breast cancer patient populations. The trial includes cohorts evaluating SY-1365 as a single agent in patients with relapsed ovarian clear cell cancer and in high-grade serous ovarian cancer (HGSOC) patients who have had three or more prior lines of therapy; in combination with carboplatin in HGSOC patients who have had one or more prior lines of therapy; in combination with fulvestrant in metastatic hormone receptor-positive breast cancer patients who are resistant to treatment with a CDK4/6 inhibitor; and as a single agent in patients with solid tumors of any histology accessible for biopsy. Additional details about the trial can be found using the identifier NCT03134638 at www.clinicaltrials.gov.

CDK7 plays a key role in the transcription of genes and in cell cycle regulation, and inhibiting CDK7 disrupts two important processes that cancer cells use to survive: 1) expression of cancer-promoting genes; and 2) uncontrolled cell cycle progression. SY-1365 has shown anti-tumor activity in preclinical models of a range of solid tumors and blood cancers, including cancers that have become resistant to treatment with existing therapies or where existing options have failed to provide meaningful benefit to patients. Further, data suggests that SY-1365 works to inhibit the growth of cell lines representing many different cancer types at nanomolar concentrations, decreases MCL1 protein levels, and demonstrates activity among cancer cells with low BCL-XL expression.

Building on its leadership in CDK7 inhibition, Syros is advancing SY-5609, a highly selective and potent oral CDK7 inhibitor, toward clinical development. In preclinical studies, SY-5609 has demonstrated substantial anti-tumor activity, including inducing complete regressions in cell line-derived xenograft models of breast and ovarian cancers. The company plans to complete investigational new drug application (IND)-enabling studies by the end of 2019 to support the initiation of a Phase 1 oncology trial in early 2020.

About Syros Pharmaceuticals
Syros is pioneering the understanding of the non-coding regulatory region of the genome to advance a new wave of medicines that control the expression of genes. Syros has built a proprietary platform that is designed to systematically and efficiently analyze this unexploited region of DNA 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 monogenic 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 SY-1365, a selective CDK7 inhibitor in a Phase 1 clinical trial focused on patients with ovarian and breast cancers. Syros is also developing a deep preclinical and discovery pipeline, including SY-5609, an oral CDK7 inhibitor, as well as programs in immuno-oncology and sickle cell disease. 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 promise of selective CDK7 inhibition and the potential benefit of SY-1365 as a therapeutic approach for difficult to treat cancers; the ability to complete IND-enabling preclinical studies and begin clinical development of SY-5609; and the benefits of Syros' gene control platform and product development pipeline. 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-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; successfully progress SY-5609 through IND-enabling preclinical and toxicology studies; 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, including its ability to perform under the collaboration agreement with Incyte; 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, 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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