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# Syros Announces New Preclinical Data on SY-1365 Showing Potent Anti-Tumor Activity in Multiple Models of Heavily Pretreated Ovarian Cancer

*Expect to Open Expansion Cohorts in Phase 1 Trial in Mid-2018, Including Cohorts Evaluating SY-1365 as a Single and Combination Agent in Multiple Ovarian Cancer Patient Populations*

*On Track to Report Data from Dose Escalation Portion of Phase 1 Trial in Fourth Quarter of 2018*

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Syros Pharmaceuticals (NASDAQ: SYRS), a biopharmaceutical company pioneering the discovery and development of medicines to control the expression of genes, today announced new preclinical data showing that SY-1365, its first-in-class selective cyclin-dependent kinase 7 (CDK7) inhibitor currently in a Phase 1 trial in patients with advanced solid tumors, demonstrated potent anti-tumor activity in multiple models of heavily pretreated ovarian cancer. These data were presented by Syros and its collaborators from the Dana-Farber Cancer Institute (DCFI) at the American Association for Cancer Research (AACR) Annual Meeting in Chicago.

“Despite recent advances in treating ovarian cancer, many patients either don’t respond or become resistant to treatment, and the outlook for these patients is poor,” said Panagiotis A. Konstantinopoulos, M.D, Ph.D., Director of Translational Research and attending oncologist in the Gynecologic Oncology Program at DCFI and an Associate Professor of Medicine at Harvard Medical School. “SY-1365 stopped tumor growth in multiple preclinical models of ovarian cancer that had progressed following treatment with standard-of-care and targeted therapies. These data suggest SY-1365 has the potential to be an important new therapy for ovarian cancer that warrants further clinical investigation.”

Researchers from Syros and DCFI evaluated the anti-tumor activity of SY-1365 in a broad panel of ovarian cancer cell lines, as well as in patient-derived xenograft (PDX) mouse models developed from patients treated with multiple prior therapies, including standard-of-care platinum-based therapies and a new class of targeted therapies known as PARP inhibitors. The data, which were presented in a poster discussion session and a poster session, show that SY-1365:

- Induced cell death in numerous ovarian cancer cell lines.
- Inhibited tumor growth in 10 of the 17 treatment-relapsed ovarian PDX models studied, including inducing complete regressions. Notably, these responses were observed irrespective of BRCA status or sensitivity to a PARP inhibitor.

- Lowered expression of *MCL1*, a gene in the mitochondrial apoptosis pathway that is known to inhibit apoptosis, or programmed cell death.

The data also showed that sensitivity to SY-1365 was associated with low expression of *BCLXL*, a known apoptosis inhibitor, and*RB1*, a known tumor suppressor, pointing to potential biomarkers that may be predictive of response to SY-1365.

“We are very encouraged by these data,” said David A. Roth, M.D., Chief Medical Officer of Syros. “CDK7 has emerged as a potentially important new drug target in cancer. By selectively inhibiting CDK7, SY-1365 has been shown to lower the expression of cancer driving genes and hit cancer cells at multiple points in the cell cycle, preferentially killing cancer cells and inhibiting tumor growth in preclinical models of a number of difficult-to-treat solid tumors and blood cancers. These newest data in ovarian cancer provide strong support for the planned expansion of our Phase 1 clinical trial into ovarian cancer and further highlight the promise of SY-1365 to make a profound difference for patients.”

The ongoing Phase 1 trial of SY-1365 is a multi-center, open-label trial enrolling patients with advanced solid tumors. 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 is open and expected to enroll approximately 35 solid tumor patients for whom standard curative or palliative measures do not exist or are no longer effective. Following the dose-escalation phase, Syros plans to open expansion cohorts to further evaluate the safety and anti-tumor activity of SY-1365 as a single agent and in combination with standard-of-care therapies in multiple ovarian and breast cancer populations.

Syros expects to open the expansion phase of the trial in mid-2018 and to report data from the dose escalation portion of the trial in the fourth quarter of 2018.

**About SY-1365**
SY-1365 is a first-in-class selective cyclin-dependent kinase 7 (CDK7) inhibitor with potential across a range of difficult-to-treat solid tumors and blood cancers. In preclinical studies, SY-1365 has shown significant anti-proliferative and pro-apoptotic activity in difficult-to-treat cancers, including breast and ovarian cancers and acute leukemia. SY-1365 has also been shown to preferentially kill cancer cells over non-cancerous cells and lower the expression of cancer-driving genes, inducing significant anti-tumor activity, including complete tumor regressions, in preclinical models of these cancers. SY-1365 is currently in a Phase 1 clinical trial in patients with advanced solid tumors, with planned expansion cohorts to evaluate SY-1365 in multiple ovarian and breast cancer patient populations as a single agent and in combination with standard-of-care therapies. Additional details about the trial can be found using the identifier NCT03134638 at www.clinicaltrials.gov.

**About Syros Pharmaceuticals**
Syros is pioneering the understanding of the non-coding region of the genome to advance a new wave of medicines that control expression of 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

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 myelodysplastic syndrome, and SY-1365, a selective CDK7 inhibitor in a Phase 1 clinical trial for patients with advanced 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 Company's ability initiate expansion cohorts in the Phase 1 clinical trial of SY-1365 in ovarian and breast cancer in mid-2018 and report data from the dose escalation portion of the trial in the fourth quarter of 2018, whether potential biomarkers of response to SY-1365 will result in a successful patient selection strategy, and the benefits of SY-1365 and 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; successfully develop a companion diagnostic test to identify patients with predictive biomarkers; 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, 2017, 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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