April 3, 2017

Syros Presents New Preclinical Data at AACR Showing Anti-Tumor Activity of SY-1365, Its First-in-Class Selective CDK7 Inhibitor, in Multiple Difficult-to-Treat Solid Tumors

– New Data Demonstrate SY-1365 Inhibits Tumor Growth in In Vivo Models of Triple Negative Breast Cancer –

– New Data Show SY-1365 Has Anti-Proliferative Activity in Additional Cancer Cells, including Ovarian and Small Cell Lung Cancers –

– New Data on CDK12 and CDK13 Inhibitor Program Highlight Company's Leadership in Transcriptional CDKs –

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, today announced that SY-1365, its first-in-class selective cyclin-dependent kinase 7 (CDK7) inhibitor, shows significant anti-proliferative 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. Leveraging its expertise in transcriptional biology and chemistry, Syros also showcased its work to further elucidate the biology of cyclin-dependent kinase 12 (CDK12) and cyclin-dependent kinase 13 (CDK13), advancing its aim of designing the first highly selective CDK12 and CDK13 inhibitors suitable for clinical development. These data were presented at the American Association of Cancer Research (AACR) Annual Meeting in Washington, D.C.

"SY-1365, our first-in-class selective CDK7 inhibitor, as well as our CDK12 and CDK13 inhibitor program highlight the power of our gene control platform to selectively target transcription and potentially treat diseases that have been underserved by other genomic-based approaches," said Nancy Simonian, M.D., Chief Executive Officer of Syros. "These new data show SY-1365 reduces proliferation and induces apoptosis in cancer cells in several difficult-to-treat tumors. The results build on earlier data demonstrating that SY-1365 preferentially kills cancer cells over non-cancerous cells and lowers the expression of disease-driving transcription factors. Our CDK12 and CDK13 inhibitor program further highlights the potential of our platform to produce drug candidates that target the transcription of unique sets of genes linked to specific tumors."

SY-1365 in Aggressive Transcriptionally Driven Solid Tumors
Data generated and presented by Syros scientists show SY-1365 induces anti-proliferative and pro-apoptotic effects in multiple solid tumor cell lines and preclinical models of

aggressive, transcriptionally driven solid tumors. Results from these studies show SY-1365:

- Induces potent anti-proliferative activity in a range of solid tumor cell lines, including triple negative breast, small cell lung and ovarian cancer cells, when profiled across a broad panel of more than 130 cancer cell lines.
- Demonstrates substantial anti-tumor activity in both cell line-derived xenograft (CDX) and patient-derived xenograft (PDX) models of triple negative breast cancer, including regressions at a twice weekly dosing regimen consistent with the initial regimen planned for the Company's upcoming Phase 1 clinical trial.
- Demonstrates synergistic anti-tumor activity with a BCL-2 inhibitor in cancer cells, providing a mechanistic rationale for further investigating SY-1365 in combination with inhibitors targeting apoptotic pathways.

SY-1365 has been previously shown to induce apoptosis and preferentially kill cancer cells over non-cancerous cells in preclinical models of a range of aggressive cancers, including certain solid tumors and acute leukemias. Preclinical studies have also shown that SY-1365 lowers the expression of oncogenic transcription factors, such as MYC, in these transcriptionally driven cancers.

Syros is on track to begin a Phase 1 clinical trial of SY-1365 in the second quarter, initially in patients with advanced solid tumor malignancies including the transcriptionally driven solid tumors, triple negative breast, small cell lung and ovarian cancers. Syros plans to expand future clinical development of SY-1365 into acute leukemias based on data generated in this trial.

CDK12 and CDK13 Inhibition as Promising New Approach for Treating Cancer
Syros scientists presented data on the selective inhibition of CDK12 and CDK13 in ovarian and breast cancers. Using its gene control platform, Syros is optimizing potent and selective CDK12 and CDK13 inhibitors that may be suitable for clinical development. Syros scientists presented data on a suite of proprietary assays capable of assessing selectivity and cellular target engagement of CDK12. Using breast and ovarian cancer cell lines sensitive to CDK12 inhibition, Syros scientists further showed important differences between non-selective and selective inhibition of transcriptional kinases to guide development of these inhibitors.

Selectively inhibiting CDK12 and CDK13 has previously been shown to decrease the expression of DNA damage response genes and super-enhancer associated transcription factors implicated in cancer, including breast and ovarian cancers. These findings suggest that a selective CDK12 and CDK13 inhibitor could be effective as a monotherapy in certain cancers and as a combination therapy in other cancers by increasing their susceptibility to targeted therapies involved in DNA damage repair, such as PARP1 inhibitors.

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 clinical development of SY-1365 and the expansion of SY-1365 clinical development into acute leukemias, the ability to create selective inhibitors of CDK12 and CDK13 that are suitable for clinical development, 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- SY-1365, 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; 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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Source: Syros Pharmaceuticals