January 8, 2018

Syros Announces 2018 Strategic Priorities and Expected Milestones

On Track to Report Clinical Data on SY-1425 Combinations and SY-1365

Initial Expansion of Phase 1 Clinical Trial of SY-1365 to Focus on Ovarian Cancer

Company Leverages Gene Control Platform for Target Discovery Collaboration with Incyte

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Syros Pharmaceuticals (NASDAQ: SYRS), a biopharmaceutical company pioneering the development of medicines to control the expression of genes, today outlined its strategic plan and expected milestones for 2018. In a presentation at the 36th Annual J.P. Morgan Healthcare Conference on Thursday, January 11, 2018, at 10:30 a.m. PST (1:30 p.m. EST), the Company will detail its three strategic priorities for the year:

- Aggressively advancing its two clinical-stage programs with planned data readouts on two combinations with SY-1425, a first-in-class selective retinoic acid receptor alpha (RARα) agonist, from the ongoing Phase 2 trial in genomically defined acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS) patients, and with the first clinical data for SY-1365, a first-in-class selective cyclin-dependent kinase 7 (CDK7) inhibitor, from the Phase 1 trial in advanced solid tumors.
- Leveraging its leading gene control platform to fuel its discovery and preclinical pipeline in oncology, including immuno-oncology, and the recent expansion into monogenic diseases, keeping the Company on track to achieve its goal of delivering one Investigational New Drug (IND) application every other year on average.
- Building on its strong fundamentals to continue its evolution toward a fully integrated biopharmaceutical company with therapies that transform patients' lives.

Syros also announced today that it has entered into a strategic collaboration and option agreement with Incyte Corporation to identify novel targets for myeloproliferative neoplasms (MPNs), a group of blood cancers in which the body makes too many white or red blood cells or platelets. Under the agreement, Syros will use its proprietary gene control platform for target discovery and validation and Incyte will be responsible for drug discovery, development and commercialization. Syros will receive $10 million upfront and a $10 million equity investment at a premium to the current market price. Syros could receive up to $54 million from Incyte in target validation and option exercise fees. Syros could receive up to $115 million in potential development, regulatory and commercial milestone payments per target for up to seven validated targets, plus low single-digit royalties on sales of products that result from the collaboration.

"We have made great strides over the past year, with data validating the ability of our platform to enrich for patients most likely to respond to SY-1425, the advancement of a

second program into clinical development, the initiation of our first program in monogenic diseases and a strategic collaboration around our leading gene control platform," said Nancy Simonian, M.D., chief executive officer of Syros. "These accomplishments position us for a transformative year in 2018 with the opportunity for multiple clinical data readouts for SY-1425 and SY-1365, a robust and growing discovery and preclinical pipeline and the continued evolution of our team and capabilities. In 2018, we are focused on continuing to execute with excellence as we strive to build a great and sustainable company that translates our leadership in gene control into therapies that provide a profound and durable benefit for patients."

Expected 2018 Milestones

SY-1425

- Report clinical data in second half of 2018 on SY-1425 in combination with azacitidine in biomarker-positive newly diagnosed AML patients who are not suitable candidates for standard chemotherapy.
- Report clinical data in second half of 2018 on SY-1425 in combination with daratumumab in biomarker-positive relapsed or refractory AML and higher-risk MDS patients. Janssen Research and Development, LLC is providing daratumumab for the clinical trial under a clinical supply agreement.

SY-1365

- Report clinical data in second half of 2018 from dose escalation phase of Phase 1 trial in advanced solid tumor patients.
- Open expansion cohorts in ovarian cancer in mid-2018 exploring SY-1365 as a single agent and in combination with carboplatin. Based on robust anti-tumor activity in multiple relapsed and refractory ovarian cancer patient-derived xenograft models, Syros plans to focus the expansion phase of the ongoing Phase 1 clinical trial on ovarian cancer with cohorts evaluating SY-1365 in multiple ovarian cancer populations as a single agent and in combination with carboplatin.

Platform and Early-Stage Pipeline

- Select a new development candidate.
- Advance discovery programs in cancer and sickle cell disease. Syros' drug discovery program in sickle cell disease is the first under its monogenic disease strategy to target gene regulatory elements to modulate the expression of a single known gene.
- Execute on target discovery work in MPNs in collaboration with Incyte.

Financial Guidance

Based on its current operating plans, Syros expects that its existing cash, cash equivalents and marketable securities, together with the upfront cash and equity investment from its collaboration with Incyte, will enable the Company to fund its anticipated operating expenses and capital expenditure requirements into 2019. Syros had approximately $81.9 million in cash, cash equivalents and marketable securities as of September 30, 2017.

Presentation at 36th Annual J.P. Morgan Healthcare Conference

Syros will webcast its corporate presentation from the 36th Annual J.P. Morgan Healthcare Conference in San Francisco on Thursday, Jan. 11, 2018, at 10:30 a.m. PST (1:30 p.m. EST). A live webcast of the presentation and question and answer session can be accessed under Events & Presentations in the News and Investors section of the Company's website at www.syros.com. A downloadable copy of the corporate slide presentation is also available on the News and Investors section of the website. A replay of the webcast will be archived on the website for approximately 30 days following the presentation.

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 advancement of the Company's clinical-stage programs, including the reporting of clinical data from the combination cohorts of the ongoing Phase 2 clinical trial of SY-1425 and the dose escalation phase of the SY-1365 clinical trial in the second half of 2018, and the initiation of expansion cohorts of SY-1365 in multiple ovarian cancer populations; the selection of a development candidate for IND-enabling studies during 2018; the advancement of the Company's preclinical programs, including programs in oncology and sickle cell disease; the Company's ability to execute in its target discovery collaboration with Incyte and receive future payments thereunder; the Company's ability to file an IND application every other year on average; the Company's cash runway; 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 whether or when Incyte will exercise any of its options or any option exercise fees, milestone payments or royalties under the Incyte collaboration will ever be paid, and Syros' ability to: advance the development of its programs, including SY-1425 and 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 the *RARA* and *IRF8* 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; the ability of our collaboration partners to satisfy their obligations under our collaboration agreements; 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’ Quarterly Report on Form 10-Q for the quarter ended September 30, 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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