November 8, 2017

Syros Reports Third Quarter 2017 Financial Results and Highlights Accomplishments and Upcoming Milestones

Presented Biomarker Data from Ongoing Phase 2 Clinical Trial of SY-1425 Demonstrating Significant Correlation Between Biomarker Status and Differentiation of Patients' Blood Cells Treated Ex Vivo

Presented PK and PD Data from Phase 2 Clinical Trial of SY-1425 Demonstrating Favorable PK and Evidence of RARα Target Engagement

Initial Clinical Data on SY-1425 as Single Agent from Relapsed or Refractory AML and Higher-Risk MDS and Lower-Risk MDS Cohorts in Phase 2 Trial to be Presented at ASH

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 reported financial results for the quarter ended September 30, 2017 and provided an update on recent accomplishments and upcoming events.

"Syros made significant progress in the third quarter, driving toward an initial clinical data readout at ASH from our ongoing Phase 2 clinical trial of SY-1425 as well as adding a combination arm with SY-1425 and an anti-CD38 therapy to the trial, and continuing to execute efficiently on the dose escalation phase of our Phase 1 trial of SY-1365," said Nancy Simonian, M.D., Chief Executive Officer of Syros. "We presented key data on both programs, showing favorable PK and evidence of target engagement in patients from the clinical trial of SY-1425, as well as a significant correlation between the biomarker status of patients screened for the trial and differentiation of their cells treated *ex vivo* with SY-1425, supporting our platform's ability to identify patients we believe may be most likely to respond to gene control therapies such as SY-1425. For SY-1365, we presented PK and PD data showing substantial anti-tumor activity in preclinical models of multiple cancers using a twice weekly dose consistent with the initial dosing regimen being used in the Phase 1 trial. We are at an exciting time in the company's evolution, with multiple clinical data readouts for SY-1425 and SY-1365 expected between now and the end of 2018, a rich preclinical pipeline, and a leading gene control platform that we believe will continue to fuel our pipeline and fulfill our mission of improving patients' lives."

Upcoming Milestones

- Syros plans to report initial clinical data from the relapsed or refractory acute myeloid leukemia (AML) and higher-risk myelodysplastic syndrome (MDS) cohort, as well as

the lower-risk transfusion-dependent MDS cohort, in its ongoing Phase 2 clinical trial of SY-1425, an oral first-in-class selective retinoic acid receptor alpha (RARα) agonist, at the 59th American Society of Hematology (ASH) Annual Meeting and Exposition on Sunday, December 10, 2017. The presentation will include data on evidence of differentiation in patients' bone marrow and initial assessments of clinical activity and safety of SY-1425 as a single agent. The Phase 2 trial is evaluating the safety and efficacy of SY-1425 as a single agent in four AML and MDS patient populations, as well as in combination with azacitidine in newly diagnosed AML patients who are not suitable candidates for standard chemotherapy. Syros recently amended the protocol of this trial to add a cohort evaluating the safety and efficacy of SY-1425 in combination with an anti-CD38 therapy in patients with relapsed or refractory AML or higher-risk MDS. The Company expects to begin enrolling patients in this cohort in early 2018. All patients enrolled or to be enrolled in the trial are prospectively selected using the Company's *RARA* and *IRF8* biomarkers.

- Syros expects to present additional clinical data from the ongoing Phase 2 trial, including data assessing the safety and efficacy of SY-1425 in combination with azacitidine and with an anti-CD38 antibody, in 2018.
- Syros plans to present new preclinical data at ASH showing significant anti-tumor activity of SY-1365, a first-in-class selective cyclin-dependent kinase 7 (CDK7) inhibitor, in multiple leukemia and lymphoma cell lines, as well as *in vivo* models of AML. The Company also plans to present preclinical data at ASH on its identification of a biomarker related to the mitochondrial apoptosis pathway that is predictive of sensitivity to SY-1365 in leukemia cell lines, as well as *in vitro* data showing synergy with the BCL2 inhibitor venetoclax.
- Syros expects to report initial clinical data from its ongoing Phase 1 trial of SY-1365 in patients with advanced solid tumors in 2018.

Recent Platform and Pipeline Highlights

- In October 2017, Syros presented preclinical PK and PD data on SY-1365 at the 2017 AACR-NCI-EORTC Molecular Targets and Cancer Therapeutics Conference. The data showed that SY-1365 has a prolonged PD effect and induces sustained tumor regressions in multiple preclinical models using intermittent dosing, supporting the twice weekly dosing regimen currently being used in the Phase 1 trial in patients with advanced solid tumors.
- In October 2017, Syros announced a publication co-authored by two of its scientific founders, Nathanael S. Gray, Ph.D., and Richard A. Young, Ph.D., in the peer-reviewed scientific journal Cancer Discovery that highlighted CDK7 inhibition in combination with targeted therapies as a promising new approach for combatting drug resistance. In multiple *in vitro* and *in vivo* models of treatment-resistant cancers, CDK7 inhibition enhanced tumor cell killing and impeded the emergence of drug-resistant cell populations when combined with targeted therapies, including MEK, BRAF, EGFR and ALK inhibitors, compared to either a CDK7 inhibitor or the targeted therapy alone.
- In October 2017, Syros' drug discovery research in immuno-oncology was highlighted in an oral presentation at the American College of Surgeons 2017 Clinical Congress. As part of a research collaboration with the Lowy laboratory at the University of

California San Diego Moores Cancer Center, Syros scientists identified alterations in regulatory regions of the genome in immune, tumor and stromal cells isolated from pancreatic cancer patient tumors. The goal of the Company's immuno-oncology program is to discover and develop new drugs with the potential to reactivate the immune system to fight cancer.

- In October 2017, Syros presented biomarker data from its ongoing Phase 2 clinical trial of SY-1425 at the European School of Haematology's 4th International Conference on Acute Myeloid Leukemia "Molecular and Translational": Advances in Biology and Treatment. The data showed that the biomarker status of patients screened for the trial was predictive of myeloid cell differentiation in the patients' blood samples treated *ex vivo* with SY-1425, supporting the potential clinical utility of the Company's biomarkers for patient selection. Data also showed that SY-1425 robustly induced CD38 in an *in vivo* model of biomarker positive AML. Syros also announced that approximately 40% of the 201 evaluable patients screened for the clinical trial through August were biomarker-positive, including one-third of relapsed or refractory AML and higher-risk MDS patients.
- In September 2017, Syros presented PK and PD data from its ongoing Phase 2 clinical trial of SY-1425 at the European Society of Medical Oncology (ESMO) 2017 Congress. The data showed that the dosing regimen being used in the trial achieves blood levels sufficient to elicit a PD response with evidence of RARα target engagement. Data also showed no significant accumulation or reduction in drug exposure after two weeks of continuous dosing, demonstrating favorable PK properties compared to historical data with ATRA, a non-selective retinoic acid receptor agonist. Syros also presented the design of its ongoing Phase 1 trial for SY-1365 at ESMO.
- In August 2017, Syros announced that the U.S. Food and Drug Administration granted orphan drug designation to SY-1425 for the treatment of AML. Orphan drug designation may provide certain benefits, including a seven-year period of market exclusivity if the drug is approved, tax credits for qualified clinical trials and an exemption from FDA application fees.

Third Quarter 2017 Financial Results

Cash, cash equivalents and marketable securities as of September 30, 2017 were $81.9 million, compared with $83.6 million on December 31, 2016. The decrease in cash, cash equivalents and marketable securities is primarily due to cash used to fund operations during the nine-months ended September 30, 2017, partially offset by gross proceeds of approximately $35.0 million from Syros' April 2017 private placement.

For the third quarter of 2017, Syros reported a net loss of $13.8 million, or $0.53 per share, compared to a net loss of $14.2 million, or $0.65 per share, for the same period in 2016. Stock-based compensation included in the net loss was $1.1 million for the third quarter of 2017, compared to $1.7 million for the same period in 2016.

- Research and development (R&D) expenses were $10.4 million for the third quarter of 2017, as compared to $11.6 million for the same period in 2016. This decrease was primarily attributable to a $1.0 million milestone payment paid to TMRC Co., Ltd. in September 2016 upon the first dosing of a patient in the Phase 2 clinical trial of SY-1425 for which no comparable payment was made in 2017, a decrease in costs from

third parties that conduct research and development and preclinical activities on the Company's behalf that are primarily due to the completion of GLP toxicology studies for SY-1365 in 2016, and a decrease in stock-based compensation. These decreases were partially offset by increases in discovery expenses. Stock-based compensation included in R&D expenses was $0.4 million for the third quarter of 2017, compared to $1.2 million for the same period in 2016.

- General and administrative (G&A) expenses were $3.6 million for the third quarter of 2017, as compared to $2.6 million for the same period in 2016. This increase was primarily attributable to an increase in employee-related costs, including salary, benefits and stock-based compensation. Stock-based compensation included in G&A expenses was $0.7 million for the third quarter of 2017, compared to $0.5 million for the same period in 2016.

Financial Guidance

Syros expects that its operating expenses for 2017 will be approximately $55.0 million. This amount includes approximately $5.0 million in non-cash expenses, primarily consisting of stock-based compensation and depreciation, resulting in an estimated cash burn of approximately $50.0 million for the year.

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 in a Phase 1 clinical trial for patients with advanced solid tumors, including transcriptionally dependent cancers such as triple negative breast, small cell lung and ovarian 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 reporting of initial clinical data from the ongoing Phase 2 clinical trial of SY-1425 at the ASH Annual Meeting; the presentation of additional clinical data on SY-1425 and initial clinical data on SY-1365; the percentage of AML and MDS patients who have the RARA or IRF8 biomarker; the benefits of CDK7 inhibition; the ability to discover and develop drugs in the immuno-oncology field that can reactivate the immune system; anticipated operating expenses and cash burn for the year ended December 31, 2017; 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. Moreover, there can be no assurance that PK and PD data and ex vivo differentiation data generated to date in the ongoing Phase 2 clinical trial of SY-1425 are predictive of the ability of such trial to meet any of its endpoints. 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-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; 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.

Syros Pharmaceuticals, Inc.
Selected Condensed Consolidated Balance Sheet Data
(in thousands)
(unaudited)

	September 30, 2017	December 31, 2016
Cash, cash equivalents and marketable securities	$ 81,948	$ 83,593
Working capital (1)	73,928	75,941
Total assets	88,677	91,323
Total stockholders' equity	78,592	80,602

(1) The Company defines working capital as current assets less current liabilities. See the Company's condensed consolidated financial statements for further details regarding its current assets and current liabilities.

Syros Pharmaceuticals, Inc.
Condensed consolidated statements of operations
(in thousands, except share and per share data)
(unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2017	2016	2017	2016
Revenue (2)	$ —	$ —	$ 1,101	$ —
Operating expenses:				
Research and development	10,447	11,584	30,116	29,374
General and administrative	3,593	2,633	10,151	7,544
Total operating expenses	14,040	14,217	40,267	36,918
Loss from operations	(14,040)	(14,217)	(39,166)	(36,918)
Other income, net	215	48	458	140
Net loss	$ (13,825)	$ (14,169)	$ (38,708)	$ (36,778)
Accrued dividends on preferred stock	—	(121)	—	(3,681)
Net loss applicable to common stockholders	$ (13,825)	$ (14,290)	$ (38,708)	$ (40,459)
Net loss per share applicable to common stockholders - basic and diluted	$ (0.53)	$ (0.65)	$ (1.54)	$ (4.44)
Weighted-average number of common shares used in net loss per share applicable to common stockholders - basic and diluted	26,259,216	22,012,743	25,100,278	9,110,993

(2) Under a research agreement we entered into with a multinational pharmaceutical company, we recognized revenue of $1.1 million during the nine months ended September 30, 2017. The research agreement expired on March 31, 2017, and we do not expect to recognize revenue from this agreement in the future. We did not earn any revenue during the nine months ended September 30, 2016.

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