November 1, 2018

Syros Reports Third Quarter 2018 Financial Results and Highlights Key Accomplishments and Upcoming Milestones

Opened Expansion Cohorts in Phase 1 Trial Evaluating SY-1365 in Multiple Ovarian and Breast Cancer Populations as Single Agent and in Combination

Selected Oral CDK7 Inhibitor SY-5609 as Development Candidate to Enter IND-Enabling Studies

Dose Escalation Data from Phase 1 Trial of SY-1365 to be Presented at EORTC-NCI-AACR and Initial Clinical Data from Combination Arms of Phase 2 Trial of SY-1425 to be Presented at ASH

Management to Host Conference Call at 7:30 AM ET Today

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Syros Pharmaceuticals (NASDAQ: SYRS), a leader in the development of medicines that control the expression of genes, today reported financial results for the quarter ended September 30, 2018 and provided an update on recent accomplishments and upcoming events.

“Syros continued to make great progress in the third quarter, marked by the achievement of two key 2018 goals: advancing SY-1365 into the expansion portion of the Phase 1 trial to evaluate it in multiple ovarian and breast cancer patient populations; and naming SY-5609, an oral selective CDK7 inhibitor, as our next development candidate,” said Nancy Simonian, M.D., Chief Executive Officer of Syros. “Together, these accomplishments speak to our leadership in gene control, as well as our belief in the transformative potential of selective CDK7 inhibition for treating a range of solid tumors and blood cancers. Looking ahead, we expect to build on our momentum as we unveil the first-ever clinical data on a selective CDK7 inhibitor from the dose escalation portion of our Phase 1 trial of SY-1365 and present initial clinical data from the combination arms of our Phase 2 trial of SY-1425.”

Upcoming Milestones:

- Syros plans to present initial clinical data from cohorts in its Phase 2 trial evaluating the safety and efficacy of SY-1425 in combination with azacitidine in *RARA* and *IRF8* biomarker-positive patients with newly diagnosed acute myeloid leukemia (AML) who are not suitable candidates for standard chemotherapy, and in combination with daratumumab in biomarker-positive patients with relapsed or refractory AML and higher-risk myelodysplastic syndrome (MDS), at the 2018 American Society of Hematology (ASH) Annual Meeting.

- Syros plans to present clinical data from the dose escalation portion of its Phase 1 trial of SY-1365 in patients with advanced solid tumors in an oral plenary session at the 30th EORTC-NCI-AACR Molecular Targets and Cancer Therapeutics Symposium on Thursday, November 15, 2018. The presentation will include data on safety, pharmacokinetics, and proof-of-mechanism using pharmacodynamic markers. In three additional presentations at EORTC-NCI-AACR, Syros plans to present new preclinical data showing the mechanistic rationale for the ongoing clinical evaluation of SY-1365 in combination with carboplatin in ovarian cancer; the first preclinical data from its oral CDK7 inhibitor program; and the discovery of drug targets and patient subsets from its analysis of the super-enhancer landscape in ovarian cancer.

Recent Pipeline Highlights:

- In October 2018, Syros selected SY-5609 as its next development candidate from a suite of internally developed, highly selective and potent oral CDK7 inhibitors. Syros is advancing SY-5609 into IND-enabling studies in oncology.
- In October 2018, Syros published preclinical data supporting its hypomethylating agent (HMA) combination development strategy for SY-1425 in *Haematologica*, a peer-reviewed journal of the European Hematology Association (EHA). The publication reviews data demonstrating the mechanistic rationale of SY-1425 in combination with HMAs in *in vitro* and *in vivo* models of AML with high *RARA* expression. SY-1425 in combination with HMAs, including azacitidine, resulted in synergistic anti-proliferative effects supported by evidence of DNA damage and apoptosis. In patient-derived xenograft models of AML with high *RARA* expression, SY-1425 in combination with azacitidine showed both greater clearance of tumor cells in bone marrow and other tissues and greater duration of response, compared to either azacitidine or SY-1425 alone.
- In September 2018, Syros advanced SY-1365 into the expansion portion of its Phase 1 trial, opening of cohorts in ovarian and breast cancer patient populations. Based on preclinical data, showing robust anti-tumor activity in ovarian and breast cancers, a strong mechanistic rationale, and high unmet need, Syros decided to focus the initial expansion of its Phase 1 trial on these tumor types. The expansion cohorts are evaluating the safety and anti-tumor activity of SY-1365 as a single agent in primary platinum-refractory ovarian cancer patients; as a single agent in ovarian cancer patients who have relapsed after three or more therapies; in combination with carboplatin in ovarian cancer patients who have relapsed after one or more prior therapies; and in combination with fulvestrant in patients with hormone-receptor positive (HR+) metastatic breast cancer who have progressed after treatment with a CDK4/6 inhibitor. An additional cohort is enrolling patients with any solid tumor accessible for biopsy to further evaluate the mechanism of action of SY-1365.

Third Quarter 2018 Financial Results

Cash, cash equivalents and marketable securities as of September 30, 2018 were $113.2 million, compared with $72.0 million on December 31, 2017.

For the third quarter 2018, Syros reported a net loss of $15.7 million, or $0.47 per share, compared to a net loss of $13.8 million, or $0.53 per share, for the same period in 2017.

- Revenues were $0.4 million for the third quarter of 2018, which relate entirely to Syros' target discovery collaboration with Incyte Corporation. Syros did not record revenues in the third quarter of 2017.
- Research and development expenses were $12.9 million for the third quarter of 2018, as compared to $10.4 million for the same period in 2017. This increase was primarily attributable to an increase in SY-1365 contract manufacturing costs and professional consulting fees in support of our clinical trials, as well as an increase in employee-related expenses.
- General and administrative expenses were $3.9 million for the third quarter of 2018, as compared to $3.6 million for the same period in 2017. This increase was primarily due to an increase in employee-related expenses.

Financial Guidance

Based on its current plans, Syros believes that its existing cash, cash equivalents and marketable securities will be sufficient to fund its planned operating expenses and capital expenditure requirements into 2020.

Conference Call and Webcast:

Syros will host a conference call today at 7:30 a.m. ET to discuss these third quarter 2018 financial results and provide a corporate update.

The live call may be accessed by dialing (866) 595-4538 for domestic callers or (636) 812-6496 for international callers and referencing conference ID number: 3988733. A live webcast of the conference call will be available online on the Investors & Media section of the Syros website at www.syros.com. An archived replay of the webcast will be available for approximately 90 days.

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 myelodysplastic syndrome, and SY-1365, a selective CDK7 inhibitor in a Phase 1 clinical trial for 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 Company's ability to advance its clinical-stage programs, including the of the timing and quantity of clinical data to be reported 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; that the reporting of data from the SY-1365 clinical trial will be the first-ever reported clinical data of a selective CDK7 inhibitor; the ability to enroll expansion cohorts in the ongoing Phase 1 clinical trial of SY-1365; the ability of SY-5609 to enter and complete IND-enabling preclinical studies; the Company's ability to fund its planned operations into 2020; 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-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; successfully progress SY-5609 through IND-enabling preclinical and toxicology studies; 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, 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, as updated in its Quarterly Reports on Form 10-Q for the quarters ended March 31, June 30 and September 30, 2018, each of 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, 2018	December 31, 2017
Cash, cash equivalents and marketable securities	$ 113,231	$ 72,049
Working capital (1)	94,247	60,746
Total assets	120,634	78,488
Total stockholders' equity	94,837	65,324

(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,	
	2018	**2017**	**2018**	**2017**
Revenue	$ 412	$ —	$ 1,157	$ 1,10
Operating expenses:				
Research and development	12,856	10,447	35,054	30,11
General and administrative	3,876	3,593	11,792	10,15
Total operating expenses	16,732	14,040	46,846	40,26
Loss from operations	(16,320)	(14,040)	(45,689)	(39,16
Other income, net	583	215	1,442	45
Net loss	$ (15,737)	$ (13,825)	$ (44,247)	$ (38,70
Net loss per share - basic and diluted	$ (0.47)	$ (0.53)	$ (1.37)	$ (1.5
Weighted-average number of common shares used in net loss per share - basic and diluted	33,653,479	26,259,216	32,306,261	25,100,27

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