August 1, 2019

Syros Reports Second Quarter 2019 Financial Results and Highlights Key Accomplishments and Upcoming Milestones

Enrollment Initiated in Phase 2 Trial Cohort Evaluating SY-1425 and Azacitidine in Genomically Defined Patients with Relapsed or Refractory Acute Myeloid Leukemia

Multiple Clinical Data Readouts Expected for SY-1425 and SY-1365 in 2019 and 2020

Management to Host Conference Call at 8:30 a.m. 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 June 30, 2019, and provided an update on recent accomplishments and upcoming events.

“This is an exciting time for Syros as we continue to advance our clinical-stage programs toward multiple data readouts this year and next that have the potential to validate our fundamental approach to drug development and catalyze change in the treatment landscape for cancers with high unmet needs,” said Nancy Simonian, M.D., Chief Executive Officer of Syros. “We plan to report updated clinical data for SY-1425 and SY-1365 in the fourth quarter, which we expect will provide additional insights into the safety and clinical activity of both drug candidates and further inform our development plans. We are particularly pleased to announce that we recently began enrolling relapsed or refractory AML patients in a new cohort in our Phase 2 trial of SY-1425 in combination with azacitidine. With this accomplishment, we now have three ongoing trial cohorts with potential for proof-of-concept data in 2020 that, if positive, bring us closer to our vision of providing much-needed therapies for patients.”

Upcoming Milestones:

SY-1425

- Syros plans to complete enrollment in the second half of 2019 in the Phase 2 trial cohort evaluating the safety and efficacy of SY-1425 in combination with azacitidine in *RARA* and *IRF8* biomarker-positive patients with newly diagnosed AML who are not suitable candidates for standard chemotherapy.
- Syros plans to report updated data on SY-1425 in combination with azacitidine in the fourth quarter of 2019 in newly diagnosed patients with AML who are not suitable candidates for standard chemotherapy.
- Syros plans to report potential proof-of-concept data from the ongoing cohort evaluating SY-1425 in combination with azacitidine in biomarker-positive patients with relapsed or refractory (R/R) AML in 2020.

SY-1365

- Syros plans to report initial clinical data in the fourth quarter of 2019 from the expansion portion of its Phase 1 trial, including: initial efficacy and safety assessments from the cohort evaluating SY-1365 as a single agent in high-grade serous ovarian cancer patients who have had three or more prior lines of therapy; initial safety and pharmacokinetic data from the cohort evaluating SY-1365 in combination with carboplatin in high-grade serous ovarian cancer patients who have had one or more prior lines of therapy; and initial safety, efficacy and mechanistic data from the cohort evaluating SY-1365 as a single agent in patients with advanced solid tumors accessible for biopsy.
- Syros plans to report additional data from these cohorts, including potential proof-of-concept data from the ongoing cohort in high-grade serous ovarian cancer patients who have had three or more prior lines of therapy, in 2020.
- Syros also plans to report potential proof-of-concept data from an ongoing cohort evaluating SY-1365 as a single agent in patients with relapsed ovarian clear cell cancer and initial data from an ongoing cohort in hormone receptor (HR)-positive CDK4/6 inhibitor-resistant breast cancer patients in 2020.

SY-5609

- Syros plans to present new preclinical data on SY-5609, including pharmacokinetic and pharmacodynamic

data and assessments of anti-tumor activity in patient-derived xenograft models of multiple cancers, in the fourth quarter.
- Syros plans to complete investigational new drug (IND)-enabling studies of SY-5609 in 2019 to support the initiation of a Phase 1 oncology trial in early 2020.

Recent Pipeline Highlights:

- In May 2019, Syros opened for enrollment the new Phase 2 trial cohort evaluating the safety and efficacy of SY-1425 in combination with azacitidine in *RARA* and *IRF8* biomarker-positive patients with R/R AML.
- In May 2019, Syros published a new manuscript, *Discovery and Characterization of SY-1365, a Selective, Covalent Inhibitor of CDK7*, in the American Association for Cancer Research's journal *Cancer Research*. The publication highlighted the discovery, mechanism of action and promise of SY-1365 as a new targeted approach to treat a range of difficult-to-treat cancers.

Recent Corporate Highlights:

- In June 2019, Syros appointed Alice Shaw, M.D., Ph.D., Director of the Center for Thoracic Cancers at Massachusetts General Hospital and a Professor of Medicine at Harvard Medical School, to its Board of Directors. Dr. Shaw is a highly respected oncologist and recognized leader in translational medicine and the development of targeted cancer therapies.

Second Quarter 2019 Financial Results:

Syros had cash, cash equivalents and marketable securities of $121.7 million as of June 30, 2019, as compared with $99.7 million in December 31, 2018. This increase in cash reflects aggregate net proceeds of approximately $65.0 million from Syros' two concurrent underwritten public offerings, which closed in April 2019.

For the second quarter of 2019, Syros reported a net loss of $19.5 million, or $0.47 per share, compared to a net loss of $14.0 million, or $0.43 per share, for the same period in 2018.

- Revenues were $0.5 million for the second quarter of 2019, as compared to $0.4 million for the second quarter of 2018. Revenues in both the second quarter of 2019 and the second quarter of 2018 were earned under Syros' collaboration with Incyte Corporation.
- Research and development (R&D) expenses were $15.5 million for the second quarter of 2019, as compared to $11.1 million for the same period in 2018. This increase was primarily attributable to continued advancement of the Company's existing clinical trials and advancement of its preclinical programs, including SY-5609 into IND-enabling studies.
- General and administrative (G&A) expenses were $5.2 million for the second quarter of 2019, as compared to $3.8 million for the same period in 2018. This increase was primarily attributable 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 to the end of the first quarter of 2021.

Conference Call and Webcast:
Syros will host a conference call today at 8:30 a.m. ET to discuss these second quarter 2019 financial results and provide a corporate update.

To access the live conference call, please dial (866) 595-4538 (domestic) or (636) 812-6496 (international), and refer to conference ID 7254685. A webcast of the call will also be available on the Investors & Media section of the Syros website at www.syros.com. An archived replay of the webcast will be available for approximately 30 days following the call.

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 SY-1365, a selective CDK7 inhibitor in a Phase 1 clinical trial focused on 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 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, quality and quantity of clinical data to be reported from the combination cohorts of the ongoing Phase 2 clinical trial of SY-1425 and the expansion phase of the ongoing Phase 1 clinical trial of SY-1365; the ability to complete enrollment in the cohort of the ongoing clinical Phase 2 clinical trial of SY-1425 in biomarker-positive newly diagnosed unfit AML patients; the ability to achieve clinical proof of concept and take advantage of fast-to-market opportunities for SY-1425 and SY-1365; the predictive value of the Company's *RARA* and *IRF8* biomarkers and develop a commercial companion diagnostic; the ability to complete IND-enabling preclinical studies and begin clinical development of SY-5609; the ability to report new preclinical data for SY-5609; the Company's ability to fund its planned operations to the end of the first quarter of 2021; 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, 2018 and Quarterly Report on Form 10-Q for the quarter ended June 30, 2019, 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)

	June 30, 2019	December 31, 2018
Cash, cash equivalents and marketable securities	$ 121,718	$ 99,679
Working capital[1]	109,036	82,205
Total assets	151,827	106,766
Total stockholders' equity	111,915	78,586

(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 June 30,	Six Months Ended June 30,

	2019	2018	2019	2018
Revenue	$ 462	$ 375	$ 916	$ 745
Operating expenses:				
Research and development	15,475	11,082	28,037	22,198
General and administrative	5,195	3,841	10,061	7,916
Total operating expenses	20,670	14,923	38,098	30,114
Loss from operations	(20,208)	(14,548)	(37,182)	(29,369)
Other income, net	753	501	1,266	859
Net loss	$ (19,455)	$ (14,047)	$ (35,916)	$ (28,510)
Net loss per share - basic and diluted	$ (0.47)	$ (0.43)	$ (0.95)	$ (0.90)
Weighted-average number of common shares used in net loss per share - basic and diluted	41,673,275	32,892,712	37,741,646	31,621,303

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