May 1, 2019

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

Successfully Completed $70 Million Financing

On Track for Multiple Data Readouts for Clinical-Stage Programs 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 March 31, 2019 and provided an update on recent accomplishments and upcoming events.

“Our first quarter accomplishments mark important progress against our strategic priorities for 2019,” said Nancy Simonian, M.D., Chief Executive Officer of Syros. “We refined our clinical development strategies for SY-1425 and SY-1365 with the aim of achieving proof-of-concept as soon as 2020 in three patient populations with high unmet needs that we believe offer opportunities for accelerated development. We presented new preclinical data supporting our mechanistic rationale for the ongoing development of SY-1365 in ovarian and breast cancers and highlighted the potency, selectivity and anti-tumor activity of SY-5609, our oral CDK7 inhibitor, further demonstrating our leadership in CDK7 inhibition. Following our successful financing in April, we believe we have sufficient funds to advance our clinical programs beyond potential proof-of-concept readouts, while continuing to execute on our long-term vision of building a fully integrated company with medicines that provide a profound benefit for patients.”

Upcoming Milestones:

SY-1425

- Syros plans to open an additional cohort in the ongoing Phase 2 trial in the third quarter of 2019 evaluating the safety and efficacy of SY-1425 in combination with azacitidine in *RARA* or *IRF8* biomarker-positive patients with relapsed or refractory acute myeloid leukemia (AML). Syros expects to report potential proof-of-concept data from this cohort in 2020 that, if positive, could enable a decision to move toward a registration study.
- Syros plans to complete enrollment in mid-2019 in the ongoing Phase 2 trial cohort evaluating the safety and efficacy of SY-1425 in combination with azacitidine in *RARA* or *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 second half of 2019 in newly diagnosed AML patients who are not suitable candidates for standard chemotherapy.

SY-1365

- Syros plans to report initial clinical data in the fourth quarter of 2019 from the expansion portion of its ongoing 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 expects 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 one or more prior lines of therapy, in 2020. Syros also expects 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 complete investigational new drug-enabling studies of SY-5609 in 2019 to support the initiation of a Phase 1 oncology trial in early 2020.

Recent Pipeline Highlights:

- In March 2019, Syros opened for enrollment the Phase 1 trial cohort evaluating SY-1365 in patients with relapsed ovarian clear cell cancer.
- In April 2019, Syros presented new preclinical data on SY-1365 at the American Association for Cancer Research (AACR) Annual Meeting. The data showed that 90 percent of high-grade ovarian cancer patient-derived xenograft models with prospectively defined RB pathway alterations responded to treatment with SY-1365. These data support the ongoing development of SY-1365 in ovarian and breast cancer patient populations that are enriched for RB pathway alterations, as well as the evaluation of these alterations as potential biomarkers of response to SY-1365.
- Also at AACR, Syros presented new preclinical data on SY-5609, demonstrating the potency, selectivity and anti-tumor activity in preclinical models of triple-negative breast cancer and ovarian cancer.

Recent Corporate Highlights:

- In April 2019, Syros announced the closing of two concurrent underwritten public offerings, which together resulted in aggregate gross proceeds from the offerings of

approximately $70 million, before deducting underwriting discounts and commissions and offering expenses of approximately $4.6 million. The offerings consisted of (i) 8,667,333 shares of Syros common stock and accompanying Class A warrants to purchase up to 1,951,844 shares of its common stock, at a combined price to the public of $7.50 per common share and accompanying Class A warrant and (ii) 666 shares of its Series A convertible preferred stock, which are convertible into 666,000 shares of its common stock, and accompanying Class A warrants to purchase up to 166,500 shares of its common stock, at a combined price to the public of $7,500 per Series A share and accompanying Class A warrant. Each Class A warrant has an exercise price of $8.625 per share and expires on October 10, 2022.

First Quarter 2019 Financial Results:

Syros had cash, cash equivalents and marketable securities of $75.9 million as of March 31, 2019, as compared with $99.7 million on December 31, 2018. Cash and cash equivalents as of March 31, 2019 do not include the net proceeds of approximately $65.4 million from the Company's April 2019 financing.

For the first quarter of 2019, Syros reported a net loss of $16.5 million, or $0.49 per share, compared to a net loss of $14.5 million, or $0.48 per share, for the same period in 2018.

- Revenues were $0.5 million for the first quarter of 2019, as compared to $0.4 million for the same period in 2018. Revenues in both the first quarter of 2019 and first quarter of 2018 were earned under Syros' collaboration with Incyte Corporation.
- Research and development (R&D) expenses were $12.6 million for the first 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 the advancement of SY-5609 into investigational new drug application (IND)-enabling studies.
- General and administrative (G&A) expenses were $4.9 million for the first quarter of 2019, as compared to $4.1 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 first 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 5435957. 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 presentation.

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 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 expansion phase of the ongoing Phase 1 clinical trial of SY-1365, as well as the opening of a new cohort in the SY-1425 trial ; 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 rapid 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 the relevance of the RB pathway alterations as potential biomarkers of response to SY-1365; the ability to complete IND-enabling preclinical studies and begin clinical development of 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, 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)

	March 31, 2019	December 31, 2018
Cash, cash equivalents and marketable securities	$ 75,866	$ 99,679
Working capital[1]	62,784	82,205
Total assets	88,428	106,766
Total stockholders’ equity	64,018	78,586

Syros Pharmaceuticals, Inc.
Condensed Consolidated Statements of Operations
(in thousands, except share and per share data)
(unaudited)

	Three Months Ended March 31,	
	2019	2018
Revenue	$ 454	$ 370
Operating expenses:		
Research and development	12,562	11,116
General and administrative	4,865	4,075
Total operating expenses	17,427	15,191
Loss from operations	(16,973)	(14,821)
Other income, net	512	358
Net loss	$ (16,461)	$ (14,463)

Net loss per share - basic and diluted	$ (0.49)	$ (0.48)
Weighted-average number of common shares used in net loss per share - basic and diluted	33,766,333	30,335,164

[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.

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Source: Syros Pharmaceuticals, Inc.