March 5, 2020

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

Initiated Phase 1 Clinical Trial of SY-5609 in Select Solid Tumors Patients

Entered into Collaboration with GBT to Advance Novel Therapies for Sickle Cell Disease and Beta Thalassemia

Well-funded with cash runway into 2022 beyond multiple expected clinical data readouts for SY-1425 and SY-5609

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 December 31, 2019, and provided an update on recent accomplishments and upcoming events.

“We are entering 2020 in a position of strength,” said Nancy Simonian, M.D., Chief Executive Officer of Syros. “Following the recent initiation of our Phase 1 trial of SY-5609, we are advancing two oral investigational medicines through development in multiple cancer patient populations that we believe are most likely to respond to these targeted agents, both with meaningful data readouts expected in the fourth quarter. Meanwhile, our gene control platform continues to fuel a robust preclinical and discovery pipeline in oncology and monogenic diseases. We are committed to executing with excellence on our ongoing efforts and, longer term, to leveraging our deep understanding of the regulatory genome to deliver much-needed medicines that provide profound benefits for patients.”

Upcoming Milestones:

SY-1425

- Report potential proof-of-concept data in the fourth quarter of 2020 from ongoing Phase 2 trial cohort evaluating SY-1425 in combination with azacitidine in RARA-positive relapsed or refractory acute myeloid leukemia (AML) patients.
- Report mature data in the fourth quarter of 2020 from fully enrolled Phase 2 trial cohorts evaluating SY-1425 in combination with azacitidine in newly diagnosed AML patients who are not suitable candidates for standard chemotherapy.

SY-5609

- Report initial safety, tolerability, pharmacokinetic (PK) and pharmacodynamic (PD) data in fourth quarter of 2020 from dose-escalation portion of Phase 1 trial evaluating SY-5609 in patients with breast, colorectal, lung and ovarian cancers, as well as in patients with solid tumors of any histology that harbor Rb pathway alterations.
- Report additional dose-escalation data, including clinical activity data, in mid-2021.

Preclinical Pipeline

- Nominate next development candidate by the end of 2021.

Recent Pipeline Highlights:

- In January 2020, Syros presented preclinical data showing that inhibiting cyclin-dependent kinase (CDK) 7 and CDK12 result in different transcriptional effects at the 2020 Keystone Symposia Cancer Epigenetics: New Mechanisms and Therapeutic Opportunities. The data showed that CDK12 inhibition preferentially decreases expression of genes with longer transcripts, a phenomenon not observed with CDK7 inhibition, pointing to distinct therapeutic opportunities for these two novel approaches to benefit patients with difficult-to-treat cancers. Also at Keystone, Syros presented on two new methods for identifying genes and transcriptional targets upon which specific cancers are particularly dependent for their survival.
- In January 2020, Syros dosed the first patient in its Phase 1 clinical trial of SY-5609. The multi-center, open-label, dose-escalation trial is expected to enroll approximately 60 patients with breast, colorectal, lung or ovarian cancer, or with solid tumors of any histology that harbor Rb pathway alterations. The primary objectives of the trial are to assess the safety and tolerability of escalating doses of SY-5609, with the goal of establishing a maximum tolerated dose. Additional objectives include assessments of anti-tumor activity, PK, PD and predictive biomarkers of response. In a future expansion portion of the trial, multiple cohorts are planned to further evaluate the safety and anti-tumor activity of SY-5609 as both a single agent and in combination with other therapies.
- In December 2019, Syros presented preclinical data demonstrating its discovery and validation of a novel fetal hemoglobin repressor, Nuclear Factor I X (NFIX) at the 61st American Society of Hematology Annual Meeting. Data showed that, when knocked down in primary cells and an erythroid cell line expressing adult hemoglobin, NFIX induced fetal hemoglobin in nearly 100% of cells and increased total fetal hemoglobin levels to 40%, exceeding levels that are associated with a functional cure in a subset of sickle cell disease (SCD) patients.
- In November 2019, Syros and its collaborators from the Whitehead Institute for Biomedical Research presented on the identification of core drivers of metastasis in triple-negative breast cancer at the 2019 San Antonio Breast Cancer Symposium.

Recent Corporate Highlights:

- In February 2020, Syros announced the closing of a $60 million senior secured loan facility with Oxford Finance, LLC. Under the terms of the financing, $20 million was drawn down at closing, and $40 million will be available across two tranches, subject to certain conditions and achievement of milestones.
- In December 2019, Syros appointed Mark Alles, the former Chairman and Chief Executive Officer of Celgene Corporation, to its Board of Directors. Mr. Alles is a

recognized biopharmaceutical executive with a proven record of building successful global oncology organizations and commercializing innovative therapies.
- In December 2019, Syros entered into a collaboration with Global Blood Therapeutics (GBT) to discover, develop and commercialize novel oral medicines for SCD and beta thalassemia. Under the agreement, Syros will use its gene control platform to identify therapeutic targets and discover drugs that induce fetal hemoglobin, and GBT will receive an option to obtain an exclusive worldwide license to develop, manufacture and commercialize products resulting from the collaboration. Under the terms of the agreement, Syros received a $20 million upfront payment. GBT is also obligated to fund up to approximately $40 million in research expenses for at least three years. Should GBT exercise its option under the agreement, Syros could receive up to $315 million in option exercise, development, regulatory, commercialization and sales-based milestones per product candidate and product resulting from the collaboration, in addition to mid- to high-single digit royalties on sales of products resulting from the collaboration.

Fourth Quarter 2019 Financial Results:

Cash, cash equivalents and marketable securities as of December 31, 2019 were $91.4 million, compared with $99.7 million on December 31, 2018. This reflects aggregate net proceeds of approximately $65 million from Syros' two concurrent underwritten public offerings, which closed in April 2019 but does not include the $20 million upfront payment received in connection with entry into collaboration with GBT or the $20 million from the initial tranche of the Oxford loan facility.

For the fourth quarter of 2019, Syros reported a net loss of $19.7 million, or $0.46 per share, compared to a net loss of $18.0 million, or $0.54 per share, for the same period in 2018.

- Revenues were $0.5 million for the fourth quarter of 2019, as compared to $0.9 million for the fourth quarter of 2018. Revenues in both the fourth quarter of 2019 and the fourth quarter of 2018 were earned under Syros' collaboration with Incyte Corporation.
- Research and development (R&D) expenses were $14.3 million for the fourth quarter of 2019, as compared to $15.1 million for the same period in 2018. This decrease was primarily attributable to the portfolio prioritization decision made during the quarter to discontinue the SY-1365 program.
- General and administrative (G&A) expenses were $6.4 million for the fourth quarter of 2019, as compared to $4.4 million for the same period in 2018. This increase was primarily attributable to an increase in employee related expenses due to increased headcount, as well as stock-based compensation expense related to the accelerated vesting of certain performance-based stock options following the execution of the Global Blood Therapeutics collaboration in December 2019.

Full Year 2019 Financial Results:

For the full year ended December 31, 2019, Syros reported a net loss of $75.4 million, or $1.88 per share, compared to a net loss of $62.3 million, or $1.91 per share, for the same period in 2018.

- Revenues were $2.0 million for the year ended December 31, 2019, as compared to $2.1 million for the same period in 2018. Revenues in both 2019 and 2018 related

entirely to the Incyte collaboration.

- R&D expenses were $58.2 million for the year ended December 31, 2019, as compared to $50.2 million for the same period in 2018. This increase was primarily attributable to the continued advancement of the Company's existing clinical trials and advancement of its preclinical programs, including completing SY-5609 IND-enabling studies.
- G&A expenses were $21.5 million for the year ended December 31, 2019, as compared to $16.2 million for the same period in 2018. This increase was primarily attributable to an increase in employee related expenses due to increased headcount.

Financial Guidance:

Based on its current plans, Syros believes that its existing cash, cash equivalents and marketable securities, including the upfront payment received in connection with the GBT collaboration and the initial tranche of the Oxford loan facility, will be sufficient to fund its planned operating expenses and capital expenditures requirements into 2022, beyond key milestones expected for both SY-1425 and SY-5609.

Conference Call and Webcast:

Syros will host a conference call today at 8:30 a.m. ET to discuss these fourth quarter and full year 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 2764269. 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 redefining the power of small molecules to control the expression of genes. Based on its unique ability to elucidate regulatory regions of the genome, Syros aims to develop medicines that provide a profound benefit for patients with diseases that have eluded other genomics-based approaches. Syros is advancing a robust pipeline, including SY-1425, a first-in-class oral selective RARα agonist in a Phase 2 trial in a genomically defined subset of acute myeloid leukemia patients, and SY-5609, a highly selective and potent oral CDK7 inhibitor in a Phase 1 trial in patients with select solid tumors. Syros also has multiple preclinical and discovery programs in oncology and monogenic diseases. For more information, visit www.syros.com and follow us on Twitter (@SyrosPharma) and LinkedIn.

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 timing for reporting and the quality of data from the ongoing clinical trial evaluating SY-1425 in combination with azacitidine in AML patients, the timing for reporting data from the Phase 1 clinical trial of SY-5609, the advancement of the Company's preclinical and discovery programs, the timing for nomination of the Company's next development candidate, the ability to draw future tranches under the Company's loan agreement with Oxford, and the sufficiency of the Company's capital resources to fund operating expense

and capital expenditure requirements into 2022 through key clinical milestones. 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-5609, 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 biomarker; 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 its collaboration agreements with Incyte Corporation and Global Blood Therapeutics; 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, 2019, 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)

	December 31, 2019	December 31, 2018
Cash, cash equivalents and marketable securities	$ 91,416	$ 99,679
Working capital[1]	90,997	82,205
Total assets	149,978	106,766
Total stockholders’ equity	79,184	78,586

1. The Company defines working capital as current assets less current liabilities. See the Company’s consolidated financial statements included in its Annual Report on Form 10-K for further details regarding its current assets and current liabilities.

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

	Three Months Ended	Year ended

	December 31,		December 31,	
	2019	2018	2019	2018
Revenue	$ 508	$ 893	$ 1,982	$ 2,050
Operating expenses:				
Research and development	14,277	15,128	58,245	50,182
General and administrative	6,402	4,372	21,478	16,164
Total operating expenses	20,679	19,500	79,723	66,346
Loss from operations	(20,171)	(18,607)	(77,741)	(64,296)
Other income, net	442	575	2,303	2,017
Net loss applicable to common stockholders	$ (19,729)	$ (18,032)	$ (75,438)	$ (62,279)
Net loss per share - basic and diluted applicable to common stockholders	$ (0.46)	$ (0.54)	$ (1.88)	$ (1.91)

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