November 5, 2020

Syros Pharmaceuticals Reports Third Quarter 2020 Financial Results and Highlights Key Accomplishments and Upcoming Milestones

Presented Initial Clinical Data from Phase 1 Study of SY-5609 at EORTC-NCI-AACR Conference

New Clinical and Translational Data for SY-1425 to be Presented at ASH Meeting

Management to Host Conference Call at 4:30 p.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 September 30, 2020, and provided an update on recent accomplishments and upcoming events.

“We are making great progress on the three pillars underlying our corporate strategy: advancing SY-1425 in RARA-positive patients, building on our leadership in CDK7 inhibition, and continuing to invest in our gene control platform to fuel a robust pipeline in oncology and monogenic diseases,” said Nancy Simonian, M.D., Chief Executive Officer of Syros. “We recently presented initial clinical data for SY-5609, our oral CDK7 inhibitor, demonstrating proof-of-mechanism and supporting our ongoing development strategy. While early, these data reinforce our conviction in CDK7 inhibition as a potentially transformative targeted approach for difficult-to-treat cancers. Looking ahead, we are eager to share new data for SY-1425 at ASH, including clinical data in two AML patient populations, which will guide next steps for the program and mark important progress toward our goal of delivering SY-1425 as a foundational therapy for all RARA-positive patients.”

Upcoming Milestones

SY-1425

- Syros plans to present new clinical data for SY-1425 at the 62nd American Society of Hematology (ASH) Annual Meeting and Exposition. In separate oral presentations, Syros will present data from the ongoing, fully enrolled Phase 2 trial cohort evaluating SY-1425 in combination with azacitidine in RARA-positive relapsed or refractory acute myeloid leukemia (AML) patients and mature data from the ongoing, fully enrolled cohort evaluating SY-1425 in combination with azacitidine in newly diagnosed unfit AML patients who are not suitable candidates for standard chemotherapy.
- Also at ASH, Syros plans to present a poster detailing new data showing that the majority of RARA-positive patients have a disease phenotype that is associated with

resistance to upfront treatment with venetoclax, further underscoring the potential of SY-1425 in combination to address an ongoing unmet need in newly diagnosed unfit AML patients.
- The abstracts for Syros' ASH presentations are now available on the ASH conference website at http://www.hematology.org/Annual-Meeting.

SY-5609

- Syros plans to report additional dose escalation data, including clinical activity data, in mid-2021.

Preclinical Pipeline

- Syros remains on track to nominate its next development candidate by the end of 2021.

Recent Pipeline Highlights

- In October 2020, Syros presented early dose-escalation data from its Phase 1 trial of SY-5609 as a single agent in patients with breast, colorectal, lung, ovarian or pancreatic cancer, or with solid tumors of any histology that harbor Rb pathway alterations, and in combination with fulvestrant in patients with CDK4/6 inhibitor-resistant HR-positive breast cancer. The data, presented at the 32nd EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics (ENA), demonstrated proof-of-mechanism at tolerable doses. Notably, increases in POLR2A mRNA expression, a PD marker being used to measure CDK7 biological activity, in patients treated at 3 mg daily reached levels associated with tumor regressions in preclinical models, as well as with CDK7 target engagement at which a clinical response and apoptosis were observed in a trial of patients with a first-generation IV CDK7 inhibitor.
  Syros recently expanded a single-agent cohort in lung cancer and the combination cohort in breast cancer to further evaluate the 3 mg daily dose in focused patient populations. Syros also opened the trial to pancreatic cancer patients and is exploring intermittent dosing regimens, with the goal of identifying optimal next steps for pursuing single-agent and combination development opportunities.

Recent Corporate Highlights

- In September 2020, Syros appointed S. Gail Eckhardt, M.D., a tenured Professor, inaugural Director of the Livestrong Cancer institutes, Chair of the Department of Oncology and Associate Dean of Cancer Programs at the University of Texas at Austin's Dell Medical School, to its Board of Directors. Dr. Eckhardt is a highly respected oncologist and a leader in targeted oncology drug development.

Third Quarter 2020 Financial Results

Cash, cash equivalents and marketable securities as of September 30, 2020 were $93.1 million, compared with $91.4 million on December 31, 2019. This increase reflects the $20 million upfront payment received in connection with Syros' entry into a collaboration with Global Blood Therapeutics, Inc. (GBT) in December 2019, the $20 million that Syros drew

down from its senior secured loan facility with Oxford Finance, LLC in February 2020, and $12.3 million from the sale of common stock under Syros' at-the-market sales facility in the first quarter. These amounts were offset with cash used to fund the Company's operations during the nine months ended September 30, 2020.

For the third quarter of 2020, Syros reported a net loss of $19.5 million, or $0.43 per share, compared to a net loss of $19.8 million, or $0.47 per share, for the same period in 2019.

- Revenues were $3.8 million for the third quarter of 2020, compared to $0.6 million for the same period in 2019. In the third quarter of 2020, $3.5 million in revenue was recognized under Syros' collaboration with GBT and $0.3 million was recognized under its collaboration with Incyte Corporation (Incyte). All revenues recognized in the third quarter of 2019 were under Syros' collaboration with Incyte.
- Research and development (R&D) expenses were $17.7 million for the third quarter of 2020, as compared to $15.9 million for the same period in 2019. This increase was primarily attributable to the continued advancement of Syros' existing clinical trials and preclinical programs, and due to increased headcount.
- General and administrative (G&A) expenses were $5.2 million for the third quarter of 2020, remaining essentially flat compared to the $5.0 million in G&A expenses recorded in the same period in 2019.

Financial Guidance

Based on its current plans, Syros believes that its existing cash and cash equivalents will be sufficient to fund its planned operating expenses and capital expenditure 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 4:30 p.m. ET to discuss its third quarter 2020 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 1088286. 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 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 and the Phase 1 clinical trial of SY-5609, the adequacy of the Company's supply chain, the advancement of the Company's preclinical and discovery programs, the timing for nomination of the Company's next development candidate, and the sufficiency of the Company's capital resources to fund operating expense and capital expenditure requirements into 2022 beyond key 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 and Quarterly Report on Form 10-Q for the quarter ended September 30, 2020, 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. In addition, the extent to which the COVID-19 outbreak continues to impact our workforce and our discovery research, supply chain and clinical trial operations activities, and the operations of the third parties on which we rely, will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the duration and severity of the outbreak, additional or modified government actions, and the actions that may be required to contain the virus or treat its impact. 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, 2020	December 31, 2019

Cash, cash equivalents and marketable securities	$ 93,133	$ 91,416
Working capital[1]	70,500	90,997
Total assets	133,335	149,978
Total stockholders' equity	45,940	79,184

(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 Statement of Operations
(in thousands, except share and per share data)
(unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2020	**2019**	**2020**	**2019**
Revenue	$ 3,828	$ 558	$ 9,394	$ 1,474
Operating expenses:				
Research and development	17,674	15,931	47,039	43,968
General and administrative	5,151	5,016	15,433	15,077
Total operating expenses	22,825	20,947	62,472	59,045
Loss from operations	(18,997)	(20,389)	(53,078)	(57,571)
Other (expense) income, net	(489)	596	(830)	1,862
Net loss applicable to common stockholders	$ (19,486)	$ (19,793)	$ (53,908)	$ (55,709)
Net loss per share - basic and diluted applicable to common stockholders	$ (0.43)	$ (0.47)	$ (1.19)	$ (1.42)

Weighted-average number of common shares used in net loss per share - basic and diluted	45,781,638	42,439,338	45,137,331	39,324,751

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