May 6, 2021

Syros Reports First Quarter 2021 Financial Results and Highlights Key Accomplishments and Upcoming Milestones

Enrolling Patients in Phase 3 Trial of SY-1425 in Combination with Azacitidine in RARA-Positive Newly Diagnosed Higher-Risk MDS Patients

Today Announced Three-Part KOL Webinar Series on Its Portfolio of Investigational Targeted Hematology Therapies, Beginning May 2021

On Track to Achieve 2021 Milestones, Including Initiation of SY-1425 and SY-2101 Clinical Trials in 2H 2021 and Additional Dose-Escalation Data for SY-5609 in 3Q 2021

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, 2021, and provided an update on recent accomplishments and upcoming events.

“We continue to make substantial progress toward our vision of building Syros into a fully integrated company, with leading portfolios in targeted hematology and selective CDK inhibition and a robust gene control discovery engine,” said Nancy Simonian, M.D., Chief Executive Officer of Syros. “We began enrolling patients in our Phase 3 clinical trial of SY-1425 in RARA-positive higher-risk MDS, marking the start of our first registration-enabling trial and an important step toward our goal of setting new standards of care in the treatment of hematologic malignancies. Looking ahead, we are poised to continue building on this momentum. We look forward to initiating additional clinical trials with SY-1425 and SY-2101 in the second half of the year and reporting new dose-escalation data, including clinical activity, from our Phase 1 trial of SY-5609 in the third quarter, while continuing to invest in our earlier-stage programs in cancer and monogenic diseases.”

Syros today announced plans to host a three-part KOL webinar series focused on its portfolio of investigational targeted hematology therapies. This series will consist of presentations from key opinion leaders and clinical collaborators who will review the unmet need and evolving landscapes in higher-risk myelodysplastic syndrome (HR-MDS), newly diagnosed unfit acute myeloid leukemia (AML), and acute promyelocytic leukemia (APL), as well as Syros leaders who will review recent progress for SY-1425 and for SY-2101 in these diseases. Each event will be webcast live on the Investors & Media section of Syros’ website, www.syros.com. More details for the series are forthcoming.

Upcoming Milestones

SY-1425: Oral RARa agonist

- Initiate randomized Phase 2 trial of SY-1425 in combination with venetoclax and azacitidine in the second half of 2021 in RARA-positive newly diagnosed AML patients who are not suitable candidates for standard intensive chemotherapy.
- Report initial data from the randomized Phase 2 trial in 2022.

SY-2101: Oral arsenic trioxide (ATO)

- Initiate dose-confirmation study of SY-2101 in the second half of 2021.
- Report confirmatory dose and pharmacokinetic data in first half of 2022.
- Initiate Phase 3 trial in patients with newly diagnosed APL in 2022.

SY-5609: Oral CDK7 inhibitor

- Report additional dose-escalation data, including clinical activity data, in the third quarter of 2021 from the ongoing Phase 1 trial of SY-5609 in patients with breast, colorectal, lung, ovarian and pancreatic cancers, as well as in patients with solid tumors of any histology harboring Rb pathway alterations.
- Initiate expansion portion of Phase 1 trial in the second half of 2021.

Gene control discovery engine

- Nominate next development candidate in 2022.

Recent Pipeline Highlights

- Syros began dosing patients in its Phase 3 trial evaluating SY-1425 in combination with azacitidine in RARA-positive patients with newly diagnosed HR-MDS. The double-blind, placebo-controlled trial is expected to enroll approximately 190 patients. Patients will be randomized 2:1 to receive SY-1425 in combination with azacitidine or placebo, respectively. The primary endpoint of the trial is complete response (CR) rate.

Recent Corporate Highlights

- In January 2021, Syros completed an underwritten public offering of 5,400,000 shares of common stock, at a public offering price of $14.00 per share, resulting in gross proceeds of approximately $75.6 million, before underwriting discounts and commissions.

First Quarter 2021 Financial Results

- Revenues were $4.8 million for the first quarter of 2021, consisting of $4.0 million in revenue recognized under Syros' collaboration with Global Blood Therapeutics, Inc. (GBT) and $0.8 million recognized under its collaboration with Incyte Corporation (Incyte). Syros recognized $2.4 million in revenue in the first quarter of 2020, including $2.2 million under its collaboration with GBT and $0.2 million under its collaboration with Incyte.
- Research and development expenses were $20.0 million for the first quarter of 2021, as compared to $14.6 million for the first quarter of 2020. This increase was primarily

attributable to the continued advancement of Syros' clinical programs, including the addition of SY-2101, and an increase in employee-related expenses.
- General and administrative (G&A) expenses were $5.7 million for the first quarter of 2021, as compared to $5.1 million for the first quarter of 2020. This increase was primarily attributable to an increase in employee-related expenses.
- For the first quarter of 2021, Syros reported a net loss of $14.2 million, or $0.23 per share, compared to a net loss of $17.2 million, or $0.39 per share, for the same period in 2020.

Cash and Financial Guidance
Cash, cash equivalents and marketable securities as of March 31, 2021 were $222.1 million, as compared with $174.0M million on December 31, 2020. This increase reflects the gross proceeds of $75.6 million that Syros received from its January 2021 public offering, partially offset by cash used to fund its operations.

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 2023.

Conference Call and Webcast
Syros will host a conference call today at 8:30 a.m. ET to discuss these first quarter 2021 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 5770919. 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 clinical-stage pipeline, including: SY-1425, a first-in-class oral selective RARα agonist in RARA-positive patients with higher-risk myelodysplastic syndrome and acute myeloid leukemia; SY-2101, a novel oral form of arsenic trioxide in patients with acute promyelocytic leukemia; and SY-5609, a highly selective and potent oral CDK7 inhibitor 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 Syros's clinical development plans, including with respect to SY-1425, SY-2101 and SY-5609, the timing of anticipated data readouts from its clinical trials, the timing of nomination of Syros's next development candidate, and the sufficiency of Syros' capital resources to fund its operating expenses and capital expenditure requirements into 2023. 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, SY-2101 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; sustain the response rates and durability of response seen to date with its drug candidates; 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; 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, 2020 and Quarterly Report on Form 10-Q for the quarter ended March 31, 2021, 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 Syros' workforce and its clinical trial operations activities, and the operations of the third parties on which Syros relies, 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)

	March 31, 2021	December 31, 2020
Cash, cash equivalents and marketable securities	$ 222,142	$ 173,984
Working capital[1]	199,308	149,933
Total assets	260,627	213,250
Total stockholders' equity	149,880	90,553

(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 March 31,	
	2021	**2020**
Revenue	$ 4,827	$ 2,379
Operating expenses:		
Research and development	20,029	14,569
General and administrative	5,739	5,149
Total operating expenses	25,768	19,718
Loss from operation	(20,941)	(17,339)
Interest income	10	384
Interest expense	(967)	(271)
Change in fair value of warrant liability	7,670	—
Net loss applicable to common stockholders	$ (14,228)	$ (17,226)
Net loss per share - basic and diluted applicable to common stockholders	$ (0.23)	$ (0.39)
Weighted-average number of common shares used in net loss per share - basic and diluted	61,379,641	43,923,999

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