May 16, 2022

Syros Pharmaceuticals Reports First Quarter 2022 Financial Results and Provides a Corporate Update

Three Data Readouts Expected in 2022:

Data from the Safety Lead-ins of the SY-5609 Trial in Pancreatic Cancer and of the SELECT-AML-1 Phase 2 Trial; Data from the Dose Confirmation Study of SY-2101 in APL

On Track to Report Data from Ongoing SELECT-MDS-1 Pivotal Trial in Q4 2023/Q1 2024

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, 2022 and provided a corporate update.

“The first quarter of 2022 was very productive for Syros as our team focused on executing across our portfolio in preparation for three data readouts this year, including from the safety lead-ins of the SY-5609 trial in pancreatic cancer and of the SELECT-AML-1 Phase 2 trial of tamibarotene as well as from the dose confirmation study of SY-2101 in APL,” said Nancy Simonian, M.D., Chief Executive Officer of Syros. “Given the current market conditions, we will not be starting the Phase 3 trial of SY-2101 until we secure additional capital. In addition, at this time we are deprioritizing the evaluation of SY-5609 in hematologic malignancies. We are focusing our resources to continue our ongoing clinical trials in order to deliver benefit to patients as well as maximize value for our shareholders.”

Tamibarotene: Oral RARα agonist

Higher-Risk Myelodysplastic Syndrome (HR-MDS)

Syros is continuing to advance the ongoing SELECT-MDS-1 Phase 3 trial in newly diagnosed RARA-positive patients with HR-MDS and remains on track to report data in the fourth quarter of 2023 or the first quarter of 2024, with a potential new drug application (NDA) filing expected in 2024.

Acute Myeloid Leukemia (AML)

Syros is evaluating tamibarotene in combination with venetoclax/azacitidine compared to venetoclax/azacitidine alone in the ongoing SELECT-AML-1 Phase 2 trial in newly diagnosed unfit RARA-positive patients with AML. Syros expects to report data, including clinical activity, from the safety lead-in portion of the study in the second half of 2022.

SY-2101: Oral arsenic trioxide (ATO)

Syros is advancing the ongoing dose confirmation trial of SY-2101 in patients with newly diagnosed acute promyelocytic leukemia (APL) and expects to announce pharmacokinetic (PK) and safety data from the trial in mid-2022. Given the current market conditions, Syros does not plan to advance SY-2101 into a Phase 3 trial until additional capital is secured.

SY-5609: Oral selective CDK7 inhibitor

Syros is evaluating SY-5609 in combination with chemotherapy in relapsed/refractory metastatic pancreatic cancer patients. The company remains on track to report data, including clinical activity, from the safety lead-in portion of the trial in the second half of 2022. Given the current market conditions, Syros is deprioritizing the development of SY-5609 for the treatment of hematologic malignancies at this time.

In addition, Roche plans for the arm of its ongoing Phase 1/1b INTRINSIC trial arm evaluating SY-5609 in combination with atezolizumab in BRAF-mutant colorectal cancer (CRC) to be open for enrollment in the first half of this year. Under the terms of Syros' agreement with Roche, Roche is the sponsor of the trial and Syros is supplying SY-5609.

Gene Control Discovery Engine

At the American Association for Cancer Research (AACR) Annual Meeting 2022, Syros presented promising CDK12 inhibitor data demonstrating strong anti-tumor activity as a single agent as well as in combination with a DNA damaging agent and a PARP inhibitor in models of breast, lung, and ovarian cancer. Additionally, the CDK12 inhibitor showed anti-tumor activity in a PARP inhibitor resistant patient-derived model (PDX) of ovarian cancer. Syros expects to nominate its next development candidate from the CDK12 inhibitor program in the second half of 2022.

First Quarter 2022 Financial Results

- Revenues were $5.5 million for the first quarter of 2022, consisting of $5.1 million in revenue recognized under Syros' collaboration with Global Blood Therapeutics, Inc. (GBT) and $0.4 million recognized under its collaboration with Incyte Corporation (Incyte). Syros recognized $4.8 million in revenue in the first quarter of 2021, consisting of $4.0 million in revenue recognized under its collaboration with GBT and $0.8 million recognized under its collaboration with Incyte.

- Research and development expenses were $25.2 million for the first quarter of 2022, as compared to $20.0 million for the first quarter of 2021. This increase was primarily due to the advancement of the Company's clinical and preclinical programs and increases in employee-related expenses due to headcount growth.

- General and administrative (G&A) expenses were $6.9 million for the first quarter of 2022, as compared to $5.7 million for the first quarter of 2021. This increase was primarily due to increases in employee-related expenses and an increase in patent prosecution costs and consulting fees.

- For the first quarter of 2022, Syros reported a net loss of $25.1 million, or $0.40 per share, compared to a net loss of $14.2 million, or $0.23 per share, for the same period in 2021.

Cash and Financial Guidance

Cash, cash equivalents and marketable securities as of March 31, 2022 were $112.9 million, as compared with $143.4 million on December 31, 2021.

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 the second quarter of 2023.

Conference Call and Webcast

Syros will host a conference call today at 8:30 a.m. ET to discuss these first quarter 2022 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 4664097. A webcast of the call will also be available on the Investors & Media section of the Syros website at. 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: tamibarotene, 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 and blood cancers. 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' clinical development plans, including with respect to tamibarotene, SY-2101 and SY-5609, Syros' ability to deliver benefit to patients and value to stockholders, the timing and impact of upcoming clinical and preclinical data readouts, the timing of nomination of Syros' next development candidate, the timing for submitting a new drug application to the FDA, the ability to secure additional capital, and the sufficiency of Syros' capital resources to fund its operating expenses and capital expenditure requirements into the second quarter of 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 tamibarotene, 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, 2021 and Quarterly Report on Form 10-Q for the quarter ended March 31, 2022, 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 pandemic 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 pandemic, 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, 2022	December 31, 2021
Cash, cash equivalents and marketable securities (current and noncurrent)	$ 112,899	$ 143,407
Working capital[1]	88,884	105,077
Total assets	152,081	182,935
Total stockholders' equity	62,742	85,218

(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,	
	2022	2021
Revenue	$ 5,467	$ 4,827
Operating expenses:		

Research and development	25,171	20,029
General and administrative	6,949	5,739
Total operating expenses	32,120	25,768
Loss from operations	(26,653)	(20,941)
Interest income	35	10
Interest expense	(976)	(967)
Change in fair value of warrant liability	2,448	7,670
Net loss applicable to common stockholders	$ (25,146)	$ (14,228)
Net loss per share applicable to common stockholders - basic and diluted	$ (0.40)	$ (0.23)
Weighted-average number of common shares used in net loss per share applicable to common stockholders - basic and diluted	63,061,423	61,379,641

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