August 5, 2021

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

Today Announced Agreement with Roche to Evaluate SY-5609 in Combination with Immunotherapy in BRAF-Mutant Colorectal Cancer Patients

Additional Dose Escalation Data for SY-5609 to be Highlighted in Oral Presentation at ESMO Congress; On Track to Advance into Phase 1 Expansion in 2H 2021

On Track to Initiate SELECT-AML-1 Randomized Phase 2 Trial of Tamibarotene in AML and Dose Confirmation Study for SY-2101 in APL in 2H 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 June 30, 2021, and provided an update on recent accomplishments and upcoming events.

“As Syros advances toward becoming a commercial-stage company, we are focused on execution across our growing portfolios in targeted hematology and selective CDK inhibition and made great strides in the second quarter,” said Nancy Simonian, M.D., Chief Executive Officer of Syros. “As announced today, we entered into an agreement with Roche to explore SY-5609 in combination with atezolizumab in colorectal cancer patients, marking the first clinical investigation of a selective CDK7 inhibitor with immunotherapy. Additionally, data from the Phase 1 dose-escalation trial of SY-5609 has been selected for an oral presentation at the ESMO Congress in September, at which time we plan to detail next steps for advancing the development of SY-5609 to further explore its potential as a novel targeted approach for difficult-to-treat cancers.”

Dr. Simonian continued, “We also continued to progress our targeted hematology portfolio with the ongoing SELECT-MDS-1 Phase 3 trial of tamibarotene in RARA-positive higher-risk MDS patients, as well as the SELECT-AML-1 randomized Phase 2 study of tamibarotene in RARA-positive unfit AML patients and our dose confirmation study of SY-2101 in APL patients, both of which are on track to start in the second half of this year. As we advance these programs through the clinic, we are engaging more deeply with the clinical community to realize the potential of tamibarotene and SY-2101 to address high unmet needs and set new standards of care in these targeted patient populations.”

Syros recently hosted a three-part key opinion leader (KOL) webinar series, reviewing both

the progress and the opportunities for tamibarotene in higher-risk myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML) and for SY-2101 in acute promyelocytic leukemia (APL). The KOLs discussed the evolving treatment landscape as well as the unmet need in these diseases. An archived replay of each KOL event can be found on the Investors & Media section of Syros' website www.syros.com.

UPCOMING MILESTONES

Targeted Hematology

Tamibarotene (formerly SY-1425): Oral RARa agonist

- Initiate SELECT-AML-1 randomized Phase 2 trial of tamibarotene 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 SELECT-AML-1 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 the first half of 2022.
- Initiate Phase 3 trial in patients with newly diagnosed APL in 2022.

Selective CDK Inhibition

SY-5609: Oral CDK7 inhibitor

- Present additional dose-escalation data, including clinical activity data, in an oral presentation at the ESMO Congress 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.
- Also at ESMO, present new preclinical data in two poster presentations, one evaluating the antitumor and pharmacodynamic activity of intermittent dosing regimens for SY-5609 in ovarian cancer models and the other evaluating SY-5609 as a single agent and in combination with chemotherapy in KRAS-mutant models.
- 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 UPDATES

- In a separate press release today, Syros announced that it has entered into an agreement with Roche, under which it will provide SY-5609 for a combination dosing cohort with atezolizumab in Roche's Phase 1/1b INTRINSIC trial. The INTRINSIC trial is evaluating multiple targeted therapies or immunotherapy as single agents or in rational specified combinations in molecularly defined subsets of colorectal cancer patients. SY-5609 will be evaluated in combination with atezolizumab in patients with BRAF-mutant disease.

- Syros also announced today that due to changes in the development landscape with the emergence of oral selective estrogen receptor degrader, or SERD, therapies, the company is no longer exploring SY-5609 in combination with fulvestrant in patients with CDK4/6 inhibitor-resistant HR-positive breast cancer.

Second Quarter 2021 Financial Results

- Revenues were $5.2 million for the second quarter of 2021, consisting of $3.3 million in revenue recognized under Syros' collaboration with Global Blood Therapeutics, Inc. (GBT) and $1.9 million recognized under its collaboration with Incyte Corporation (Incyte). Syros recognized $3.2 million in revenue in the second quarter of 2020, including $2.5 million under its collaboration with GBT and $0.7 million under its collaboration with Incyte.
- Research and development expenses were $25.8 million for the first quarter of 2021, as compared to $14.8 million for the second quarter of 2020. This increase was primarily attributable to the advancement of Syros' clinical programs and an increase in employee-related expenses.
- General and administrative (G&A) expenses were $5.5 million for the second quarter of 2021, as compared to $5.1 million for the second quarter of 2020. This increase was primarily attributable to increased employee-related expenses.
- For the second quarter of 2021, Syros reported a net loss of $22.5 million, or $0.36 per share, compared to a net loss of $17.2 million, or $0.38 per share, for the same period in 2020.

Cash and Financial Guidance

Cash, cash equivalents and marketable securities as of June 30, 2021 were $195.3 million, as compared with $174 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 second 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 4156527. 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: 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. 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 June 30, 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 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)

	June 30, 2021	December 31, 2020
Cash, cash equivalents and marketable securities (current and noncurrent)	$195,293	$ 173,984
Working capital[1]	158,584	149,933
Total assets	233,734	213,250
Total stockholders' equity	129,977	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 June 30,		Six Months Ended June 30,	
	2021	2020	2021	2020
Revenue	$ 5,162	$ 3,188	$ 9,989	$ 5,566
Operating expenses:				
Research and development	25,786	14,796	45,815	29,365
General and administrative	5,520	5,133	11,260	10,282
Total operating expenses	31,306	19,929	57,075	39,647
Loss from operations	(26,144)	(16,741)	(47,086)	(34,081)
Interest income	12	32	24	416
Interest expense	(969)	(487)	(1,937)	(757)
Change in fair value of warrant liability	4,611	—	12,281	—
Net loss applicable to common stockholders	$ (22,490)	$ (17,196)	$ (36,718)	$ (34,422)
Net loss per share applicable to common stockholders - basic and diluted	$ (0.36)	$ (0.38)	$ (0.59)	$ (0.77)
Weighted-average number of common shares used in net loss per share applicable to common stockholders - basic and diluted	62,859,500	45,699,277	62,123,658	44,811,638

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