November 5, 2021

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

First Patient Dosed in SELECT-AML-1 Trial of Tamibarotene and in Dose Confirmation Study of SY-2101 in APL

Presented Phase 1 Data of SY-5609 at ESMO, Demonstrating Clinical Activity at Tolerable Doses and Supporting Development in Three Combination Regimens

Expanded Leadership Team with Key Appointments

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 September 30, 2021, and provided an update on recent accomplishments and upcoming events.

“Syros made significant progress this quarter as we executed on important milestones across our portfolios in targeted hematology and CDK inhibition as well as strengthened our leadership team with the additions of Conley Chee as Chief Commercial Officer and Jason Haas as Chief Financial Officer,” said Nancy Simonian, M.D., Chief Executive Officer of Syros. “In September, we dosed the first patient in our SELECT-AML-1 Phase 2 trial of tamibarotene, as well as in our dose confirmation study of SY-2101 in APL. Taken together, these accomplishments mark important progress toward potentially offering new standards of care for people living with hematologic cancers and showcase our commitment to building a robust and synergistic portfolio in targeted hematology.”

Dr. Simonian continued, “Building on our leadership in selective CDK7 inhibition, we presented encouraging clinical data from our Phase 1 trial of SY-5609. The data demonstrated proof-of-activity across multiple difficult-to-treat tumors and suggest that we have identified an optimal dosing schedule for further development. Based on these results, we plan to evaluate SY-5609 as part of a three-pronged combination strategy in areas of high unmet need that are supported by strong mechanistic rationale and clinical or pre-clinical activity. We expect to initiate an expansion cohort in pancreatic cancer as well as a Phase 1b trial in mantle cell lymphoma in the fourth quarter of 2021 and the first half of 2022, respectively, and look forward to working with Roche to evaluate SY-5609 in combination with its PDL1 inhibitor in BRAF-mutant colorectal cancer.”

UPCOMING MILESTONES

Targeted Hematology

Tamibarotene: Oral RARa agonist

- Report initial data from SELECT-AML-1 trial in 2022.

SY-2101: Oral arsenic trioxide (ATO)

- Report confirmatory dose and pharmacokinetic data from the dose confirmation trial in the first half of 2022.
- Initiate Phase 3 trial in newly diagnosed APL patients in 2022.

CDK Inhibition

SY-5609: Oral Selective CDK Inhibitor

- Initiate expansion cohort of our SY-5609 trial in combination with chemotherapy in second-line pancreatic cancer in the fourth quarter of 2021.
- Initiate Phase 1b trial evaluating SY-5609 in combination with a Bruton's tyrosine kinase (BTK) inhibitor for the treatment of mantle cell lymphoma in the first half of 2022.

Gene Control Discovery Engine

- Nominate next development candidate in 2022.

RECENT PIPELINE HIGHLIGHTS

- In September, Syros dosed the first patient in its dose confirmation study of SY-2101. The study is designed to evaluate the safety, tolerability, and pharmacokinetics of SY-2101 and is expected to enroll up to 24 newly diagnosed APL patients.
- Also in September, Syros dosed the first patient in its SELECT-AML-1 Phase 2 trial to evaluate the safety and efficacy of tamibarotene in combination with venetoclax and azacitidine. Following a safety lead-in, approximately 80 patients will be randomized 1:1 to receive tamibarotene in combination with venetoclax and azacitidine, or venetoclax and azacitidine alone. The primary endpoint is composite complete response rate.
- At the 2021 ESMO Congress in September, Syros presented new data from its Phase 1 trial of SY-5609 in heavily pretreated patients with select-solid tumors, which demonstrated clinical activity at tolerable doses as a single agent across multiple tumor types:
    - Thirteen patients achieved stable disease (SD) with tumor regressions of up to 20% in six of those patients, across multiple tumor types.
    - The most substantial clinical activity was observed in heavily pre-treated patients with advanced pancreatic cancer. Five of 13 of these evaluable patients achieved SD, with tumor reductions in two of those patients.
    - Across all doses and schedules, the majority of adverse events were low-grade and reversible.
    - Optimal dosing regimen of 7 days on/7 days off was identified for further evaluation.
- Based on these data along with pre-clinical data, strong mechanistic rationale, and high unmet need, Syros is evaluating SY-5609 in a three-pronged combination

approach:
    - Combination with chemotherapy for the treatment of pancreatic cancer.
    - Combination with a BTK inhibitor for the treatment of mantle cell lymphoma.
    - Combination with PDL1 inhibitor for the treatment of BRAF-mutant colorectal cancer. As previously disclosed, Syros entered into an agreement with Roche to explore this combination in Roche's Phase 1/1b INTRINSIC trial.

RECENT CORPORATE HIGHLIGHTS

- In October, Syros appointed Jason Haas as Chief Financial Officer. Jason brings more than 25 years of healthcare investment banking and corporate finance experience.
- In September, Syros appointed Conley Chee as the Company's first Chief Commercial Officer. Conley brings 20 years of pharmaceutical sales leadership, marketing, and strategy experience.
- Also in September, Syros appointed Deborah Dunsire, M.D., a highly respected industry veteran, to the Board of Directors.

THIRD QUARTER 2021 FINANCIAL RESULTS

- Revenues were $5.7 million for the third quarter of 2021, consisting of $5.6 million in revenue recognized under Syros' collaboration with Global Blood Therapeutics, Inc. (GBT) and $0.1 million recognized under its collaboration with Incyte Corporation (Incyte). Syros recognized $3.8 million in revenue in the third quarter of 2020, including $3.5 million under its collaboration with GBT and $0.3 million under its collaboration with Incyte.
- Research and development expenses were $27.3 million for the third quarter of 2021, as compared to $17.7 million for the third quarter of 2020. This increase was primarily due to the continued advancement of Syros' clinical and preclinical programs and an increase in employee-related expenses.
- General and administrative (G&A) expenses were $5.3 million for the third quarter of 2021, as compared to $5.2 million for the third quarter of 2020.
- For the third quarter of 2021, Syros reported a net loss of $26.0 million, or $0.41 per share, compared to a net loss of $19.5 million, or $0.43 per share, for the same period in 2020.

Cash and Financial Guidance

Cash, cash equivalents and marketable securities as of September 30, 2021 were $166.7 million, as compared with $174 million on December 31, 2020. This reflects cash used to fund Syros' operations during the nine months ended September 30, 2021, partially offset by gross proceeds of $75.6 million that Syros received from its January 2021 public offering.

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 third 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 3287324. 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 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, the potential for Syros' clinical programs to result in new standards of care, the timing of anticipated data readouts from its clinical trials, the timing of nomination of Syros' 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 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, 2020 and Quarterly Report on Form 10-Q for the quarter ended September 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)

	September 30, 2021	December 31, 2020
Cash, cash equivalents and marketable securities (current and noncurrent)	$ 166,701	$ 173,984
Working capital[1]	123,391	149,933
Total assets	208,043	213,250
Total stockholders' equity	106,060	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 September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Revenue	$ 5,697	$ 3,828	$ 15,686	$ 9,394
Operating expenses:				
Research and development	27,262	17,674	73,077	47,039
General and administrative	5,346	5,151	16,606	15,433
Total operating expenses	32,608	22,825	89,683	62,472
Loss from operations	(26,911)	(18,997)	(73,997)	(53,078)
Interest income	32	4	56	421
Interest expense	(984)	(493)	(2,921)	(1,251)
Change in fair value of warrant liability	1,836	—	14,117	—

Net loss applicable to common stockholders	$ (26,027)	$ (19,486)	$ (62,745)	$ (53,908)
Net loss per share applicable to common stockholders - basic and diluted	$ (0.41)	$ (0.43)	$ (1.01)	$ (1.19)
Weighted-average number of common shares used in net loss per share applicable to common stockholders - basic and diluted	62,928,299	45,781,638	62,394,819	45,137,331

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