March 2, 2023

Syros Reports Fourth Quarter and Full Year 2022 Financial Results and Provides a Corporate Update

-- Commenced randomized portion of SELECT-AML-1 trial, with initial data expected in 4Q 2023 --

-- Received FDA Fast Track designation for tamibarotene for the treatment of HR-MDS --

-- On-track to complete enrollment in SELECT-MDS-1 trial in 4Q 2023, with pivotal data expected in 3Q 2024 --

-- Management to host conference call at 8:30 a.m. ET today --

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Syros Pharmaceuticals (NASDAQ:SYRS), a biopharmaceutical company committed to advancing new standards of care for the frontline treatment of hematologic malignancies, today reported financial results for the quarter and full-year ended December 31, 2022 and provided a corporate update.

“In 2022, we advanced our efforts to develop new standards of care for the frontline treatment of hematologic malignancies, announcing promising data from our ongoing studies in AML and APL and progressing our pivotal trial in HR-MDS,” said Nancy Simonian, M.D., Chief Executive Officer of Syros. “We believe we are well-positioned to build on this progress in the year ahead. We are also encouraged by the continued momentum in our global enrollment for SELECT-MDS-1. As evidenced by the FDA’s recent decision to grant Fast Track Designation to tamibarotene for HR-MDS, there is a clear need for new therapies that can address the needs of people living with this progressive and devastating disease and we are working with urgency, together with physicians around the world, to recruit and enroll the SELECT-MDS-1 trial. In addition, we have initiated the randomized portion of the SELECT-AML-1 Phase 2 trial and are actively screening patients. We expect to report initial data from SELECT-AML-1 in the fourth quarter of this year and to provide an update on the development path and timing for further evaluation of SY-2101 in a registration-enabling study in APL in the second half of this year.”

Dr. Simonian continued, “Following our strategic financing in 2022, we are operating from a position of financial strength, with sufficient capital to fund our efforts into the second quarter of 2025. Importantly, we expect that this capital will bring us beyond Phase 3 data from the SELECT-MDS-1 trial and initial data from the randomized portion of the SELECT-AML-1 trial, while also allowing us to begin investing in the commercial infrastructure that will be necessary to deliver our products to patients.”

UPCOMING MILESTONES

Tamibarotene: Higher-Risk Myelodysplastic Syndrome (HR-MDS)

- Complete patient enrollment in the SELECT-MDS-1 Phase 3 trial in newly diagnosed HR-MDS patients with *RARA* gene overexpression in the fourth quarter of 2023.
- Report pivotal complete response (CR) data from the SELECT-MDS-1 Phase 3 trial in the third quarter of 2024.

Tamibarotene: Acute Myelodysplastic Syndrome (AML)

- Announce initial data from the randomized portion of the SELECT-AML-1 Phase 2 trial in newly diagnosed unfit AML patients with *RARA* overexpression in the fourth quarter of 2023.
- Report additional data from the SELECT-AML-1 Phase 2 trial in 2024.

SY-2101: Acute Promyelocytic Leukemia (APL)

- Provide an update on the dose confirmation study of SY-2101, as well as the development path and timing for further evaluation of SY-2101 in a registration-enabling study in APL, in the second half of 2023.

RECENT PIPELINE HIGHLIGHTS

- Initiated the randomized portion of the SELECT-AML-1 study and patient screening. The study is designed to evaluate the safety and efficacy of tamibarotene in combination with venetoclax and azacitidine compared to venetoclax and azacitidine in approximately 80 patients with *RARA* overexpression, randomized 1:1. The primary endpoint is composite complete response (cCR) rate.
- In February 2023, the U.S. Food and Drug Administration (FDA) granted Fast Track Designation to tamibarotene for the treatment of HR-MDS. Fast Track is a process designed by the FDA to facilitate the development and expedite the review of drugs that have the potential to treat serious conditions and address recognized areas of unmet medical need.
- In December 2022, Syros announced the publication in *Blood Advances* of results from the completed biomarker-directed Phase 2 trial of tamibarotene in combination with azacitidine in newly diagnosed unfit AML patients. In patients with *RARA* gene overexpression, the combination of tamibarotene and azacitidine demonstrated a cCR rate of 61%, with a rapid onset and clinically meaningful durability. In patients with low blast count AML, the CR rate was 67%. In addition, correlative analyses of *RARA* expression levels identified an association of *RARA* overexpression with a monocytic gene expression signature that may be associated with resistance to venetoclax. Together, these data support Syros' ongoing evaluation of tamibarotene for the treatment of AML and MDS patients with *RARA* overexpression.
- At the 64th American Society for Hematology (ASH) Annual Meeting in December 2022, Syros presented data from six response-evaluable patients in the safety lead-in portion of the ongoing SELECT-AML-1 Phase 2 trial. Treatment with the triplet combination of tamibarotene, venetoclax and azacitidine in patients with *RARA* overexpression demonstrated an 83% cCR rate and rapid onset of action, with no evidence of increased toxicity relative to historical data of the venetoclax and azacitidine doublet combination.
- In December 2022, Syros also extended the research term under the collaboration

agreement with Global Blood Therapeutics (GBT), now a part of Pfizer, for an additional year.

Fourth Quarter and Full Year 2022 Financial Results

- Revenues were negative $0.8 million for the fourth quarter of 2022, as compared to $7.8 million in the fourth quarter in 2021. This decrease reflects a cumulative catch-up adjustment of revenue recognized under Syros' collaboration with GBT as a result of extending the term of the research collaboration by one year. Revenues were $14.9 million for the year ended December 31, 2022, consisting of $13.6 million and $1.3 million from Syros' collaborations with GBT and Incyte, respectively and $23.5 million for the year ended December 31, 2021.
- Research and development expenses were $27.9 million for the fourth quarter of 2022 and $111.9 million for the year ended December 31, 2022, as compared to $26.8 million for the fourth quarter of 2021 and $99.9 million for the year ended December 31, 2021. The increase for the fourth quarter of 2022 compared to the same period in 2021 and the increase for the year ended December 31, 2022 compared to the year ended December 31, 2021 were primarily due to the increase in costs associated with the continued advancement of our clinical programs and employee-related expenses.
- General and administrative (G&A) expenses were $7.3 million for the fourth quarter of 2022 and $29.3 million for the year ended December 31, 2022, as compared to $6.4 million for the fourth quarter of 2021 and $23.0 million for the year ended December 31, 2021.
- Transaction-related expenses of $9.5 million for the year ended December 31, 2022 primarily consist of incurred costs allocated to the warrants issued in connection with the PIPE financing that were accounted for as liabilities, and severance paid to former Tyme employees following our acquisition of Tyme in September 2022.
- For the fourth quarter of 2022, Syros reported a net loss of $4.8 million, or $0.17 per share, compared to a net loss of $23.8 million, or $3.78 per share, for the same period in 2021. For the full year ended December 31, 2022, Syros reported a net loss of $94.7 million, or $7.49 per share, compared to a net loss of $86.6 million, or $13.84 per share, for the same period in 2021.

Cash and Financial Guidance

Cash, cash equivalents and marketable securities as of December 31, 2022 were $202.3 million, as compared with $143.4 million on December 31, 2021.

Based on its current plans, Syros believes that its existing cash, cash equivalents and marketable securities will be sufficient to fund its anticipated operating expenses and capital expenditure requirements into the second quarter of 2025, beyond Phase 3 data from the SELECT-MDS-1 trial and initial data from the randomized portion of the SELECT-AML-1 trial.

Conference Call and Webcast

Syros will host a conference call today at 8:30 a.m. ET to discuss these fourth quarter and full year 2022 financial results and provide a corporate update.

To access the live conference call, please dial (888) 575-5167 (domestic) or (416) 764-8687

(international) and refer to conference ID 74534085. 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 committed to developing new standards of care for the frontline treatment of patients with hematologic malignancies. Driven by the motivation to help patients with blood disorders that have largely eluded other targeted approaches, Syros is advancing a robust late-stage clinical pipeline, including tamibarotene, a first-in-class oral selective RARα agonist in patients with higher-risk myelodysplastic syndrome and acute myeloid leukemia with *RARA* gene overexpression, and SY-2101, a novel oral form of arsenic trioxide in patients with acute promyelocytic leukemia. Syros is also seeking partnerships for SY-5609, a highly selective and potent CDK7 inhibitor in clinical development for the treatment of select solid tumors, and multiple preclinical 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 the progression of its clinical trials and the timing and impact of opening clinical sites, enrolling study participants and reporting clinical data, the ability to deliver benefit to patients, the potential benefits of receiving Fast Track designation, and the sufficiency of Syros' capital resources to fund its operating expenses and capital expenditure requirements into the second quarter of 2025. 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 and SY-2101, 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, 2022, 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.

Syros Pharmaceuticals, Inc.
Selected Condensed Consolidated Balance Sheet Data
(in thousands)
(unaudited)

	December 31, 2022	December 31, 2021
Cash, cash equivalents and marketable securities (current and noncurrent)	$ 202,304	$ 143,407
Working capital	180,614	105,077
Total assets	244,486	182,935
Total stockholders' equity	127,736	85,218

Syros Pharmaceuticals, Inc.
Condensed Consolidated Statement of Operations
(in thousands, except share and per share data)
(unaudited)

	Three Months Ended December 31,		Year Ended December 31,	
	2022	2021	2022	2021
Revenue	$ (754)	$ 7,802	$ 14,880	$ 23,488
Operating expenses:				
Research and development	27,914	26,796	111,944	99,872
General and administrative	7,329	6,429	29,199	23,036
Transaction related expenses	0	0	9,510	0
Total operating expenses	35,243	33,225	150,753	122,908
Loss from operations	(35,997)	(25,423)	(135,873)	(99,420)
Interest income	1,594	31	2,132	87
Interest expense	(1,126)	(986)	(4,134)	(3,907)
Change in fair value of warrant liability	30,756	(2,565)	43,221	16,682
Net loss applicable to common stockholders	$ (4,773)	$ (23,813)	$ (94,654)	$ (86,558)
Net loss per share applicable to common stockholders - basic and diluted	$ (0.17)	$ (3.80)	$ (7.49)	$ (13.80)
Weighted-average number of common shares used in net loss per share applicable to common stockholders - basic and diluted	27,753,257	6,259,088	12,631,968	6,553,497

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