

November 14, 2022



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

Closed Merger with TYME Technologies and Concurrent PIPE; Proceeds from Combined Transactions Augment Cash Balance, Ending Third Quarter with Approximately \$245 Million and Extending Cash Runway into 2025

Initial Data from Safety Lead-in Portion of SELECT-AML-1 Phase 2 Trial to be Presented at ASH

Initial Data from Safety Lead-in of Phase 1 Trial of SY-5609 Demonstrates Encouraging Safety and Clinical Activity in Pancreatic Cancer Patients

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, 2022 and provided a corporate update.

“The third quarter was transformative for Syros. In September, we announced the closing of our merger with TYME Technologies and concurrent oversubscribed PIPE, with combined gross proceeds of approximately \$190 million,” said Nancy Simonian, M.D., Chief Executive Officer of Syros. “With this additional capital, we believe we are well-positioned to build Syros into a commercial-stage company. We are now focused on advancing our late-stage hematology programs toward important clinical milestones, beginning with the presentation of initial results, including clinical activity, from the safety lead-in portion of the SELECT-AML-1 Phase 2 trial at the ASH Annual Meeting in December. In addition, we remain on track to report data from the pivotal SELECT-MDS-1 trial in late 2023 or early 2024 and, based on the preliminary data from our dose confirmation study of SY-2101 that we announced in August, expect to initiate a Phase 3 trial in patients with APL in the second half of next year.”

Dr. Simonian continued, “Today, we are excited to announce initial data from the safety lead-in portion of our Phase 1 trial evaluating SY-5609 in combination with chemotherapy in patients with relapsed/refractory metastatic pancreatic cancer as well as an update from the single agent portion in advanced solid tumor patients. Importantly, the data reinforce our belief in the promise of selective CDK7 inhibition to benefit many difficult to treat cancers. To maximize the potential of SY-5609, we made the strategic decision to seek partnership opportunities for this program while we continue dose escalation in the ongoing trial, and to focus our internal resources on advancing our late-stage hematology portfolio for the frontline treatment of MDS, AML and APL.”

UPCOMING MILESTONES

Tamibarotene: Oral RAR α agonist

Higher-Risk Myelodysplastic Syndrome (HR-MDS)

- On track to report pivotal data from the SELECT-MDS-1 trial in newly diagnosed HR-MDS patients with *RARA* gene overexpression in the fourth quarter of 2023 or the first quarter of 2024, with a potential new drug application (NDA) filing expected in 2024.

Acute Myelodysplastic Syndrome (AML)

- Present safety and clinical activity data from the safety lead-in portion of the ongoing SELECT-AML-1 Phase 2 trial in newly diagnosed unfit AML patients with *RARA* overexpression at the 64th American Society of Hematology (ASH) Annual Meeting in December. The presentation, titled “Initial Results from SELECT-AML-1, a Phase 2 study of Tamibarotene in Combination with Venetoclax and Azacitidine in *RARA*-positive Newly Diagnosed AML Patients Ineligible for Standard Induction Chemotherapy,” is scheduled to be presented in a poster session on December 10, 2022.
- Expect to initiate the randomized portion of the SELECT-AML-1 Phase 2 trial in an additional eighty patients evaluating the triplet regimen of tamibarotene, venetoclax and azacitidine compared to venetoclax and azacitidine with data expected in 2023 or 2024.

SY-2101: Oral arsenic trioxide (ATO)

- Expect to initiate the Phase 3 trial of SY-2101 in patients with newly diagnosed acute promyelocytic leukemia (APL) in the second half of 2023.

RECENT PIPELINE HIGHLIGHTS

- Today, Syros announced initial safety and clinical activity data from the safety lead-in portion of the ongoing Phase 1 trial evaluating SY-5609 in combination with chemotherapy in patients with relapsed/refractory metastatic Pancreatic Ductal Adenocarcinoma (PDAC) as well as from the ongoing single agent portion in relapsed/refractory patients with select solid tumors. The data showed:
 - As of October 12, 2022, SY-5609 was generally safe with enhanced tolerability being maintained in the 7 day on/ 7 day off regimen at the highest doses evaluated to date, up to 10 mg when administered as a single agent, up to 5 mg when administered in combination with gemcitabine, and up to 4 mg when administered with gemcitabine/nab-paclitaxel.
 - The single agent 10 mg dose level did not result in any dose limiting toxicities (DLTs), further supporting the tolerability of the 7 day on/7 day off dosing regimen in which 30 patients have been dosed across five dose levels (4, 5, 6, 7, and 10 mg), with only one DLT observed at the 4 mg single agent dose level.
 - A maximum tolerated dose (MTD) has not yet been reached in either the single agent or in the chemotherapy combination cohorts in the 7 day on/ 7 day off dosing regimen. The adverse event profile of SY-5609 in combination with chemotherapy was consistent with the safety profile of single agent SY-5609 or

gemcitabine monotherapy or gemcitabine/nab-paclitaxel, and the majority of adverse events were low grade and reversible, with no new safety signals identified.

- The most common related adverse events in the cohort with SY-5609 and gemcitabine, where the highest SY-5609 doses were evaluated in combination with chemotherapy, included fatigue, nausea, decreased appetite and decreased platelet count (all low grade), with one patient experiencing a DLT of grade 3 diarrhea at the 5 mg SY-5609 dose level. No DLTs were reported in patients treated with SY-5609 in combination with gemcitabine/nab-paclitaxel.
- As of October 20, 2022, in the single agent cohort at 10 mg of SY-5609, two of three enrolled patients with select solid tumors were response evaluable, including one patient with PDAC and one with Colorectal Cancer both achieved stable disease (SD). The one patient with PDAC with SD experienced a 10% tumor reduction.
- In the cohort evaluating the doublet combination of SY-5609 and gemcitabine in patients with PDAC, one of four (25%) response evaluable patients treated at the 4 mg SY-5609 dose level experienced a confirmed partial response (PR) with a 98% reduction in the CA 19-9 tumor marker from a baseline of 60,357 U/mL to 968 U/mL, and three of four (75%) response evaluable patients treated at the 5 mg SY-5609 dose level had SD, for an overall disease control rate (DCR) of 50% (4 of 8 patients).
- Data from the doublet and the 10 mg single agent dose support an emerging exposure-response relationship; notably, the patient with the PR demonstrated higher-than-average exposure relative to other patients at that dose.
- In the cohort evaluating the triplet combination of SY-5609 and gemcitabine/nab-paclitaxel in PDAC patients, one of two response evaluable patients treated at the 4 mg dose level achieved SD.

Syros plans to continue dose escalation of SY-5609 to 15 mg as a single agent and to 10 mg in the gemcitabine combination cohort and in parallel, will be seeking a partnership for further development of SY-5609.

- In September, the U.S. Food and Drug Administration (FDA) granted Orphan Drug Designation to SY-5609 for the treatment of pancreatic cancer. The FDA's Office of Orphan Drug Products grants orphan status to support development of medicines for the treatment of rare diseases that affect fewer than 200,000 people in the United States. Orphan drug designation may provide certain benefits, including a seven-year period of market exclusivity if the drug is approved, tax credits for qualified clinical trials and an exemption from FDA application fees.

CORPORATE

- In September, Syros announced the closing of its merger with TYME Technologies, pursuant to which Syros acquired TYME, including its pipeline assets and net cash at closing of approximately \$60 million. Concurrent with the closing of the merger, Syros also closed the previously announced oversubscribed \$130 million private investment in public equity (PIPE) financing. New and existing investors in the PIPE, which was led by a life-sciences focused investment fund, include Syros co-founder and founding investor Flagship Pioneering, Avidity Partners, Deep Track Capital, Bain Capital Life

Sciences, Invus, Samsara BioCapital, Adage Capital Partners LP, Ally Bridge Group and Cowen Healthcare Investments, as well as other investors.

Third Quarter 2022 Financial Results

- Revenues were \$3.9 million for the third quarter of 2022, consisting of \$3.7 million in revenue recognized under Syros' collaboration with Global Blood Therapeutics, Inc. (GBT), now a subsidiary of Pfizer, and \$0.2 million recognized under its collaboration with Incyte. Syros recognized \$5.7 million in revenue in the third quarter of 2021, consisting of \$5.6 million in revenue recognized under its collaboration with GBT and \$0.1 million recognized under its collaboration with Incyte.
- Research and development expenses were \$25.8 million for the third quarter of 2022, as compared to \$27.3 million for the third quarter of 2021. This decrease was primarily due to a decrease in external costs related to our preclinical programs.
- General and administrative (G&A) expenses were \$8.1 million for the third quarter of 2022, as compared to \$5.3 million for the third quarter of 2021. This increase was primarily due to employee-related expenses and recruiting fees.
- Transaction related expenses were \$9.5 million for the third quarter of 2022 and consisted of the PIPE financing transaction cost allocated to warrant classified liabilities and severance paid to former Tyme employees.
- For the third quarter of 2022, Syros reported a net loss of \$30.3 million, or \$3.21 per share, compared to a net loss of \$26 million, or \$4.14 per share, for the same period in 2021.

Cash and Financial Guidance

Cash, cash equivalents and marketable securities as of September 30, 2022 were \$244.5 million, as compared with \$143.4 million on December 31, 2021.

Syros expects that its existing cash, cash equivalents and marketable securities will be sufficient to fund its planned operating expenses and capital expenditure requirements into 2025.

Conference Call and Webcast

Syros will host a conference call today at 8:30 a.m. ET to discuss these third quarter 2022 financial results and provide a corporate update. Participants may register for the conference call [here](#). While not required, it is recommended that participants join the call ten minutes prior to the scheduled start.

A live webcast of the call will also be available on the Investors & Media section of the Syros website at <http://ir.syros.com>. An archived replay of the webcast will be available for approximately 30 days following the call.

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 RAR α agonist in patients with higher-risk myelodysplastic syndrome and acute myeloid leukemia with *RARA* gene overexpression; 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](https://twitter.com/SyrosPharma)) and [LinkedIn](https://www.linkedin.com/company/syros-pharma).

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, the timing and impact of upcoming clinical and preclinical data readouts, the timing for submitting a new drug application to the FDA, the ability to develop into a commercial-stage company, the benefits of receiving an orphan drug designation for SY-5609, the intention to seek a partnership for SY-5609, and the sufficiency of Syros' capital resources to fund its operating expenses and capital expenditure requirements into 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, 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 September 30, 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.

This press release contains hyperlinks to information that is not deemed to be incorporated

by reference in this press release.

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

	September 30, 2022	December 31, 2021
Cash, cash equivalents and marketable securities (current and noncurrent)	\$ 244,481	\$ 143,407
Working capital	213,881	105,077
Total assets	284,725	182,935
Total stockholders' equity	129,171	85,218

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,	
	2022	2021	2022	2021
Revenue	\$ 3,891	\$ 5,697	\$ 15,634	\$ 15,686
Operating expenses:				
Research and development	25,759	27,262	84,030	73,077
General and administrative	8,076	5,346	21,970	16,606
Transaction related expenses	9,510	—	9,510	—
Total operating expenses	43,345	32,608	115,510	89,683
Loss from operations	(39,454)	(26,911)	(99,876)	(73,997)
Interest income	392	32	539	56
Interest expense	(1,051)	(984)	(3,008)	(2,921)
Change in fair value of warrant liability	9,860	1,836	12,465	14,117
Net loss applicable to common stockholders	\$ (30,253)	\$ (26,027)	\$ (89,880)	\$ (62,745)
Net loss per share applicable to common stockholders - basic and diluted	\$ (3.21)	\$ (4.14)	\$ (11.93)	\$ (10.06)
Weighted-average number of common shares used in net loss per share applicable to common stockholders - basic and diluted	9,417,069	6,292,830	7,536,149	6,239,482

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