UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): January 08, 2024

Syros Pharmaceuticals, Inc.
(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-37813**	**45-3772460**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**
35 CambridgePark Drive 4th Floor Cambridge, Massachusetts		**02140**
(Address of Principal Executive Offices)		**(Zip Code)**

Registrant's Telephone Number, Including Area Code: (617) 744-1340

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001 per share	SYRS	The Nasdaq Global Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

From time to time, Syros Pharmaceuticals, Inc. (the "Company") intends to conduct meetings with third parties in which its current corporate slide presentation is presented. A copy of this slide presentation, dated January 2024, is furnished as Exhibit 99.1 to this Current Report on Form 8-K. The information responsive to Item 7.01 of this Form 8-K and Exhibit 99.1 hereto shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934 (the "Exchange Act") or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933 or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 8.01 Other Events.

On January 8, 2024, the Company issued a press release announcing its 2024 anticipated milestones. The full text of this press release is filed as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated herein by reference. The information contained on the websites referenced in the press release is not incorporated herein.

Item 9.01 Financial Statements and Exhibits.

Exhibit No.	Description
99.1	Slide presentation, dated January 2024
99.2	Press release, dated January 8, 2024
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Syros Pharmaceuticals, Inc.

Date: January 8, 2024

By: /s/ Jason Haas
Jason Haas
Chief Financial Officer

Exhibit 99.1

SYROS

Advancing Novel Treatments for Hematologic Malignancies

JP Morgan Conference
January 2024

Forward-looking statements

This presentation contains forward-looking statements (including within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, and Section 27A of the Securities Act of 1933, as amended) concerning Syros and other matters, such as Syros' clinical development plans, including with respect to tamibarotene, Syros' ability to deliver benefit to patients and value to stockholders, the timing and impact of upcoming enrollment milestones and clinical data readouts, and the sufficiency of Syros' capital resources to fund its operating expenses and capital expenditure requirements into the second quarter of 2025. These statements may discuss goals, intentions and expectations as to future plans, trends, events, results of operations or financial condition, or otherwise, based on management's current beliefs, as well as assumptions made by, and information currently available to, management. Forward-looking statements generally include statements that are predictive in nature and depend upon or refer to future events or conditions, and include words such as "may," "will," "should," "would," "expect," "anticipate," "plan," "likely," "believe," "estimate," "project," "intend," and other similar expressions. Statements that are not historical facts are forward-looking statements. Forward-looking statements are based on current beliefs and assumptions that are subject to risks and uncertainties and are not guarantees of future performance. Actual results could differ materially from those contained in any forward-looking statement as a result of various factors, including, without limitation, Syros' ability to: advance the development of its programs, including tamibarotene, 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 out-licensing arrangements 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. The foregoing review of important factors that could cause actual events to differ from expectations should not be construed as exhaustive and should be read in conjunction with statements that are included herein and elsewhere, including the risk factors included in Syros' Annual Report on Form 10-K for the year ended December 31, 2022 and Syros' Quarterly Report on Form 10-Q for the quarter ended September 30, 2023, each of which is on file with the Securities and Exchange Commission (SEC). Except as required by applicable law, Syros undertakes no obligation to revise or update any forward-looking statement, or to make any other forward-looking statements, whether as a result of new information, future events or otherwise.

Advancing our vision to deliver on the value of tamibarotene

Now

Advancing tamibarotene as a potential new standard of care for HR-MDS and AML patients with *RARA* gene overexpression

Preparing for product launch and commercialization

Cash runway to fund planned operations into Q2 of 2025

Vision

Commercial company delivering new standard of care for frontline treatment of hematologic malignancies

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Advancing Tamibarotene:

Potential to establish new standard of care for the frontline treatment of hematologic malignancies

ENCOURAGING, CONSISTENT DATA FROM MULTIPLE CLINICAL TRIALS SUPPORT DEVELOPMENT STRATEGY

Growing body of evidence in MDS and AML patients with *RARA* overexpression

MEANINGFUL NEAR-TERM CATALYSTS

Upcoming opportunities to build momentum and create value: pivotal SELECT-MDS-1 data and additional randomized SELECT-AML-1 data, both expected in 2024

LARGE MARKET OPPORTUNITIES IN FRONTLINE SETTINGS

Building a focused infrastructure to support targeted patient populations underserved by existing options

$45M FINANCING ADDS TO STRONG CORPORATE POSITION:
CASH RUNWAY TO FUND OPERATIONS INTO Q2 OF 2025

Multiple near-term value-driving milestones and pre-launch activities underway

Tamibarotene
in newly diagnosed HR-MDS

Last patient enrolled for the pivotal CR data from SELECT-MDS-1 Phase 3 trial	**1Q 24**
Pivotal data from SELECT-MDS-1 Phase 3 trial	**By mid-4Q 24**

Tamibarotene
in newly diagnosed unfit AML

Initial data from randomized SELECT-AML-1 trial	✓ **Dec. 2023**
Additional data from randomized SELECT-AML-1 trial	**2024**

Pre-launch
activities

- Educating and preparing the treatment community for tamibarotene and *RARA* overexpression
- Planning distribution and sales infrastructure
- Partnered with Qiagen to ensure *RARA* testing availability at launch

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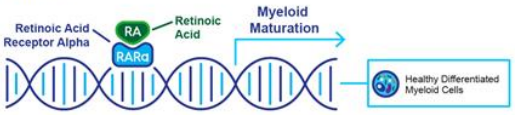
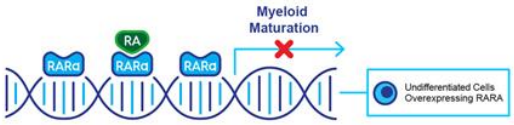
Tamibarotene: Compelling profile that addresses large targeted populations

Tamibarotene is a **selective and potent** RARα agonist[1]

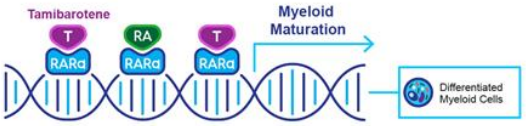
Normal



***RARA* overexpression without tamibarotene**



***RARA* overexpression with tamibarotene**



~50% of patients with HR-MDS are positive for *RARA* overexpression[2]

~30% of patients with AML are positive for *RARA* overexpression[2]

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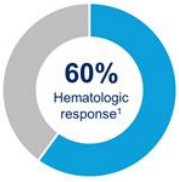
[1]McKeown, Cancer Discovery 2017; [2]de Botton S., et al. Blood Advances 2022

Growing body of clinical evidence for tamibarotene in HR-MDS and AML patients with *RARA* overexpression supports development strategy

2017

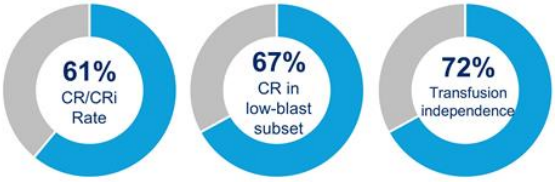
Single-agent tamibarotene in R/R HR-MDS patients[1]



including one marrow CR

2020

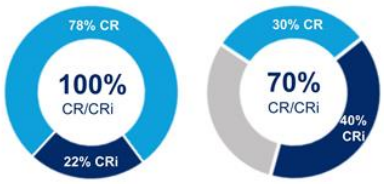
Phase 2 data evaluating Tami/Aza in ND unfit AML patients[2]



Median time to response[3]: **1.2 months**
Median duration of response: **10.8 months**
Overall survival for complete responders: **18 months**

2023

Phase 2 initial **randomized** data evaluating Tami/Ven/Aza vs. Ven/Aza in ND unfit AML patients[4]



Tami/Ven/Aza Median time to response: **21 days**

Tamibarotene in HR-MDS | Tamibarotene in AML

[1]Data presented at ASH 2017, and Syros Data on File; [2]de Botton S., et al. Blood Advances 2022; [3]Response includes CR, CRi or CRh; [4]Data presented by Syros 06Dec2023

Tamibarotene has demonstrated a well-tolerated safety profile

Safety profile supports use of tamibarotene in combination with azacitidine in MDS and with venetoclax/azacitidine in AML

Well-characterized in over 1,000 acute promyelocytic leukemia (“APL”) patients treated with tamibarotene[1]	Single agent in AML and MDS patients and doublet (Tami/Aza) in AML patients[2,3]	Triplet (Tami/Ven/Aza) in AML patients[4,5]

- Daily dosing of tamibarotene as a single-agent and in combination with azacitidine has been generally well-tolerated.[2-5]
  - No evidence of increased toxicity in combination, with rates of myelosuppression comparable to single-agent azacitidine.[2-5]
- As a triplet, myelosuppression has been comparable to venetoclax + azacitidine[4,5]
- The majority of non-hematologic AEs have been low grade and reversible[2-5]

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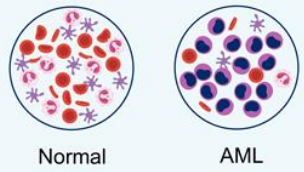
[1]Amnolake® post-marketing surveillance data on file; [2]Data presented at ASH 2017; [3]de Botton S., et al. Blood Advances 2022; [4]Data presented at ASH 2022; [5]Data presented by Syros 06Dec2023

Significant unmet need in newly diagnosed unfit AML



- Acute myeloid leukemia (AML) is a cancer of the blood forming cells in the bone marrow
- ~50% of the patients are not eligible for intensive treatment and are considered “unfit”[1]

The standard of care falls short, underscoring the critical demand for improved treatments for newly diagnosed unfit AML patients

- Venetoclax with azacitidine is standard of care, with a **66%** CR/CRi, **37%** CR rate and median OS of **14.7** months[2]
- Approximately **1/3** of patients do not respond, and nearly all relapse with a very poor prognosis, median OS of **2.4** months[3]

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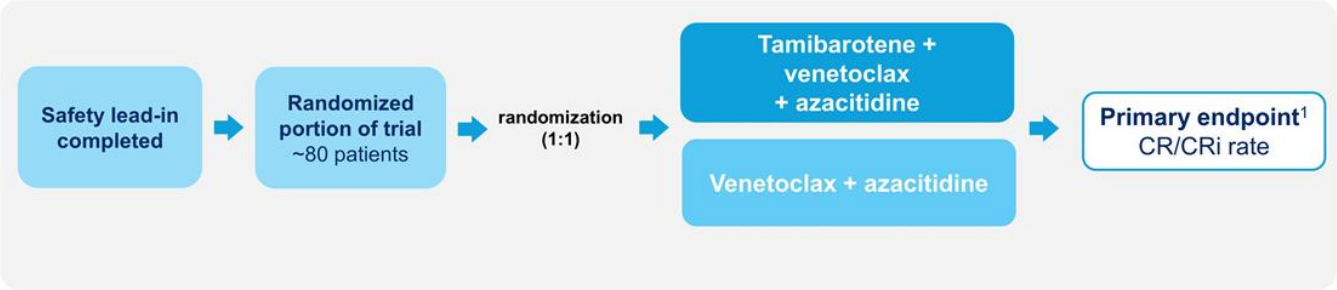
[1] Ferrara F., Clin Lymphoma Myeloma Leuk. 2011; [2]DiNardo CD, et al., New England Journal of Medicine, 2020; [3]Maiti A., et al., Haematologica, 2021.

Ongoing SELECT-AML-1 Phase 2 trial of triplet regimen (Tami/Ven/Aza) in newly diagnosed unfit AML patients with *RARA* overexpression



Key Milestones	
Initial randomized SELECT-AML-1 clinical data from 23 enrolled patients^	✓
Additional data from randomized SELECT-AML-1 trial	**2024**

[1] The study is 80% powered to detect a difference between the CR/CRi rates in the experimental and control arms
^ Data presented by Syros 06Dec2023; Data cut-off was November 13, 2023

Initial randomized SELECT-AML-1 Phase 2 data in newly diagnosed unfit AML patients with *RARA* overexpression demonstrate 100% CR/CRi rate

Initial randomized data builds on previous reported data from the safety lead-in:

TREATMENT ARM: Tami/Ven/Aza

CR/CRi Rate
100%

CR Rate
78%

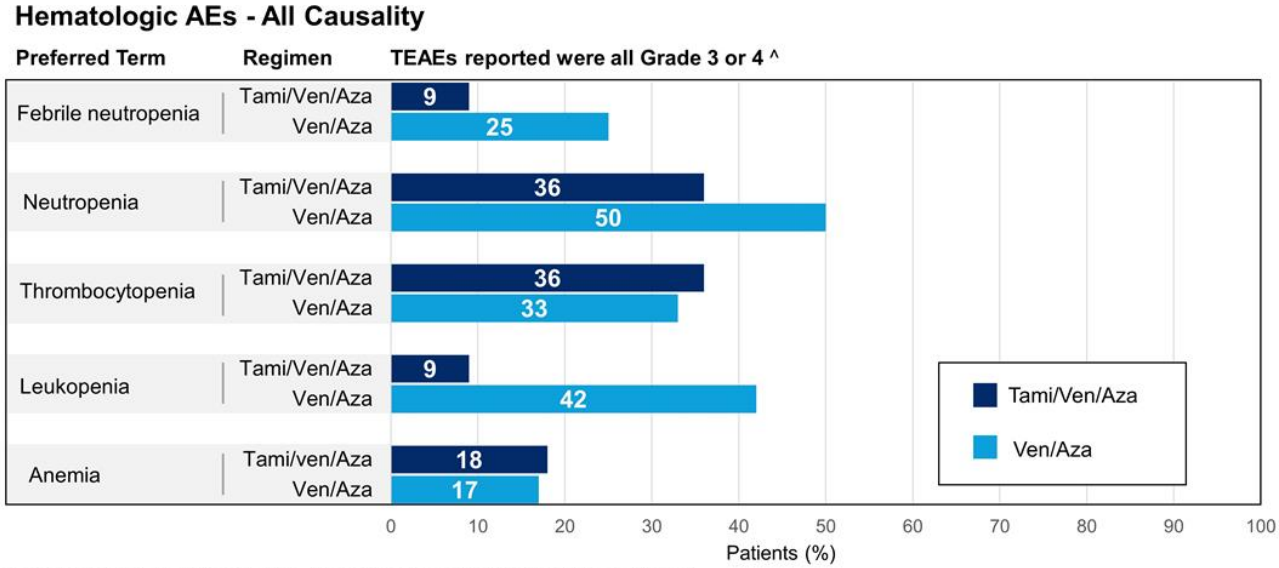
CONTROL ARM: Ven/Aza

CR/CRi Rate
70%

CR Rate
30%

Tamibarotene in combination with venetoclax and azacitidine was **well tolerated with no new safety signals identified**

Initial randomized SELECT-AML-1 Phase 2 data: Hematologic safety profile shows no additive myelosuppression when combining tamibarotene with Ven/Aza



Tami/Ven/Aza Safety Population, N=11; Ven/Aza Safety Population, N=12*

* Includes 1 patient randomized to Tami/Ven/Aza who received Ven/Aza and discontinued treatment prior to receiving tamibarotene.
^ No low-grade (Grade 1/Grade 2) Hematology AEs were reported for patients in either arm of the study.

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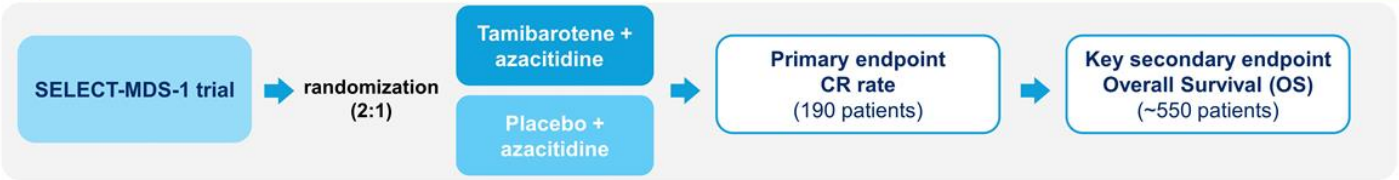
Higher-Risk MDS (HR-MDS) is closely related to AML

- Myelodysplastic syndrome (MDS) is also a cancer of the blood forming cells in the bone marrow
- HR-MDS often is a precursor to AML. More than half of HR-MDS patients progress to AML[1]
- Azacitidine, a hypomethylating agent (HMA), is SOC with a **17% CR rate** and a median OS of **18.6 months**[2]
- There is a **significant need for new therapies** - no new therapies beyond HMAs approved since 2006

"MDS-excess blasts" and "AML" essentially form a continuum…Rather than blast percentage, disease categorization may be more accurate if based on biologic features." – Estey et al., 2022[3]

[1] Greenberg, Blood, 2012; [2]Garcia, J et al., Leukemia Research, 2021; [3]Elihu Estey, et al., Blood 2022

Ongoing SELECT-MDS-1 Phase 3 trial in newly diagnosed HR-MDS patients with *RARA* overexpression



- Robustly designed, double-blind, placebo-controlled study
- 2:1 randomization
- Global study with over 120 sites recruiting in 13 countries
- FDA feedback supports:
  - Focus on population with *RARA* overexpression
  - CR as primary endpoint for approval (full or accelerated) with supporting data on durability of remission
  - Azacitidine as appropriate comparator
- Primary endpoint of CR rate is over 90% powered to detect a difference between experimental and control arms with a one-sided alpha of 0.025
- Inclusion of OS key secondary endpoint will allow this single trial to efficiently serve as a confirmatory study if needed for full approval
- Fast Track Designation by the FDA

Key Milestones

Last patient enrolled for the pivotal CR data from SELECT-MDS-1 Phase 3 trial	**1Q 24**
Pivotal data from SELECT-MDS-1 Phase 3 trial	**by mid-4Q 24**

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Planning our commercial launch in the United States

- Experienced leadership team with proven capabilities and expertise in launching targeted oncology medicines
- Planning our distribution and sales infrastructure strategy for a launch in the U.S.
- Targeted patient populations will allow for a focused, specialized sales force
- Partnered with Qiagen to ensure *RARA* testing availability

Large market opportunities in frontline settings

Building infrastructure to target synergistic patient populations underserved by existing options

MYELODYSPLASTIC SYNDROME (MDS)

~21,000 Newly Diagnosed HR-MDS patients in the US and EU annually[1]

PROJECTED MDS GLOBAL MARKET BY 2028:

~$4.7B[3]

ACUTE MYELOID LEUKEMIA (AML)

~25,000 Newly Diagnosed Unfit AML patients in US and EU annually[2]

PROJECTED AML GLOBAL MARKET BY 2028:

~$7.5B[4]

[1]Epidemiology projections from DRG Myelodysplastic Syndromes-Landscape & Forecast-Report 2020 and from DRG Acute Myelogenous Leukemia-Landscape & Forecast-Report 2020; [2]Epidemiology projections from DRG Acute Myelogenous Leukemia-Landscape & Forecast-Report 2020; [3]Evaluate Pharma global market estimate includes all risk groups for MDS; [4]Global market estimate includes all AML (fit and unfit)

Multiple near-term value-driving milestones and pre-launch activities underway

Tamibarotene
in newly diagnosed HR-MDS

Last patient enrolled for the pivotal CR data from SELECT-MDS-1 Phase 3 trial	**1Q 24**
Pivotal data from SELECT-MDS-1 Phase 3 trial	**by mid-4Q 24**

Tamibarotene
in newly diagnosed unfit AML

Initial data from randomized SELECT-AML-1 trial	✓ **Dec. 2023**
Additional data from randomized SELECT-AML-1 trial	**2024**

Pre-launch
activities

- Educating and preparing the treatment community for tamibarotene and *RARA* overexpression
- Planning distribution and sales infrastructure
- Partnered with Qiagen to ensure *RARA* testing availability at launch

SYROS


SYROS

Exhibit 99.2

Syros Highlights Anticipated 2024 Milestones to Deliver on the Value of Tamibarotene

— On-Track to Complete Enrollment of 190 patients for Primary Analysis inSELECT-MDS-1 Phase 3 Trial in 1Q 2024; Pivotal CR Data Expected by Mid-4Q 2024 —

— Additional Data from SELECT-AML-1 Phase 2 Trial Expected in 2024; Initial Data Demonstrated 100% CR/CRi Rate and Favorable Tolerability Profile —

— Strengthened Balance Sheet with Gross Proceeds of Approximately $45.0 Million from Recent Equity Financing, Extending Cash Runway into 2Q 2025 —

CAMBRIDGE, Mass., January 8, 2024 – Syros Pharmaceuticals (NASDAQ:SYRS), a biopharmaceutical company committed to advancing new standards of care for the frontline treatment of hematologic malignancies, today highlighted anticipated 2024 milestones to deliver on the value of tamibarotene.

"We are beginning the year with tremendous momentum toward our mission of delivering tamibarotene as a new standard of care for the frontline treatment of hematologic malignancies," said Conley Chee, Chief Executive Officer of Syros Pharmaceuticals. "Last month, we announced encouraging initial data from the randomized portion of the SELECT-AML-1 Phase 2 trial, which demonstrated a 100% CR/CRi rate and favorable tolerability, strongly supporting continued development in AML and HR-MDS. In addition, we closed an approximately $45.0 million equity financing, providing us additional capital to advance the development of tamibarotene. We are continuing pre-launch activities, including efforts to drive awareness of tamibarotene and of *RARA* overexpression in support of a future launch."

Mr. Chee continued, "Following these achievements, we are preparing for an important transformation. By the middle of the fourth quarter of 2024, we expect to report pivotal data from the SELECT-MDS-1 Phase 3 clinical trial. If successful, these data will allow us to file our first New Drug Application and, ultimately, to deliver tamibarotene to the thousands of HR-MDS patients in need of better options. We also plan to report additional data from SELECT-AML-1, which we expect will build on our growing body of clinical evidence and continue to demonstrate a highly differentiated product profile. We look forward to these major milestones as we work to deliver better outcomes to the many HR-MDS and AML patients with *RARA* overexpression."

Program Updates and Expected Milestones

Syros is developing tamibarotene, an oral, first-in-class selective retinoic acid receptor alpha (RARα) agonist for the frontline treatment of higher-risk myelodysplastic syndrome (HR-MDS) and acute myeloid leukemia (AML) in patients with *RARA* gene overexpression. Syros believes tamibarotene – a biologically targeted agent that has demonstrated high complete response rates, a rapid time to response and favorable tolerability across multiple clinical trials to date – has the potential to set a new standard of care for patients with *RARA* overexpression, which accounts for approximately 50 percent of the HR-MDS and 30 percent of the AML populations.

Syros is currently evaluating tamibarotene in combination with azacitidine in newly diagnosed HR-MDS patients with *RARA* overexpression in the ongoing SELECT-MDS-1 Phase 3 trial. The primary endpoint of SELECT-MDS-1 is the complete response (CR) rate. Syros expects to complete enrollment of the 190 patients necessary to support the CR primary endpoint analysis in the first quarter of 2024 and to report pivotal CR data by the middle of the fourth quarter of 2024.

Syros is also evaluating tamibarotene in combination with venetoclax and azacitidine in newly diagnosed unfit AML patients with *RARA* overexpression. In December, Syros announced encouraging initial data from the ongoing randomized SELECT-AML-1 Phase 2 trial, demonstrating a 100% CR/CRi rate in response-evaluable patients treated with the triplet regimen of tamibarotene, venetoclax and azacitidine, as compared to 70% among patients treated with venetoclax and azacitidine alone. The median time to CR/CRi response was rapid; all patients treated with the triplet regimen achieved a CR/CRi by the end of cycle one. Consistent with prior clinical experience reported last

year, tamibarotene in combination with approved doses of venetoclax and azacitidine was generally well tolerated, and the overall safety profile demonstrated no additive toxicities or new safety signals, and no evidence of increased myelosuppression compared to treatment with the doublet combination of venetoclax and azacitidine. Syros expects to report additional data from SELECT-AML-1 in 2024.

Financial Guidance

Based on its current operating plans, and including gross proceeds of approximately $45.0 million received in its December 2023 equity offering before underwriting discounts and commissions and offering expenses, Syros expects 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 the Phase 3 data from the SELECT-MDS-1 trial and additional data from SELECT-AML-1.

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 developing tamibarotene, an oral selective RARα agonist in frontline patients with higher-risk myelodysplastic syndrome and acute myeloid leukemia with *RARA* gene overexpression. 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 involving tamibarotene and related pre-launch activities, the timing and impact of upcoming clinical data readouts, the timing to complete enrollment of the 190 patients necessary to support the CR primary endpoint analysis in SELECT-MDS-1, the therapeutic potential of tamibarotene, 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 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 and Quarterly Report on Form10-Q for the quarter ended September 30, 2023, 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.

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