INVESTOR FACT SHEET
Updated 3/31/2023

OUR MISSION AND FOCUS
Syros is a biopharmaceutical company committed to developing new standards of care for the frontline treatment of hematologic malignancies. Driven by the motivation to help patients with blood disorders that have largely eluded other targeted approaches, Syros is advancing a late-stage clinical pipeline in hematology, with ongoing programs in myeloid dysplastic syndrome, acute myeloid leukemia and acute promyelocytic leukemia.

HEMATOLOGY FOCUSED LATE-STAGE CLINICAL PIPELINE

<table>
<thead>
<tr>
<th>Program</th>
<th>Indication</th>
<th>Early Clinical</th>
<th>Mid-clinical</th>
<th>Pivotal</th>
<th>Commercial Rights</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tamibarotene</td>
<td>(Newly diagnosed HR-MDS (w/aza))</td>
<td>Phase 3 SELECT-MDS-1</td>
<td></td>
<td></td>
<td>SYROS Americas, Europe, Australia and Israel</td>
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<tr>
<td>(oral RARα agonist)</td>
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<tr>
<td>Tamibarotene</td>
<td>(Newly diagnosed unfit AML (w/ven+aza))</td>
<td>Phase 2 SELECT-AML-1</td>
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<tr>
<td>SY-2101</td>
<td>(oral ATO agonist)</td>
<td>PK and Dose confirmation study</td>
<td></td>
<td></td>
<td>SYROS</td>
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<tr>
<td>(Newly diagnosed APL (w/ATRA))</td>
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MARKET OPPORTUNITY

MYELODYSPLASTIC SYNDROME (MDS)
~21,000 Newly diagnosed HR-MDS patients in the US and EU annually

PROJECTED MDS MARKET BY 2026:
~$3.3B

ACUTE MYELOID LEUKEMIA (AML)
~25,000 Newly diagnosed Unfit AML patients in the US and EU annually

PROJECTED NEWLY DIAGNOSED AML MARKET BY 2025:
~$6.6B

MULTIPLE VALUE-DRIVING MILESTONES

<table>
<thead>
<tr>
<th>Program</th>
<th>Event Description</th>
<th>Timeframe</th>
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</thead>
<tbody>
<tr>
<td>Tamibarotene</td>
<td>Last patient enrolled for the primary endpoint analysis from SELECT-MDS-1 Phase 3 trial</td>
<td>4Q 23</td>
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<tr>
<td>in HR-MDS</td>
<td>Pivotal data for complete response (CR) from SELECT-MDS-1 Phase 3 trial</td>
<td>3Q 24</td>
</tr>
<tr>
<td>Tamibarotene</td>
<td>Initial data from randomized SELECT-AML-1 trial</td>
<td>4Q 23</td>
</tr>
<tr>
<td>in AML</td>
<td>Additional data from randomized SELECT-AML-1 trial</td>
<td>2024</td>
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<tr>
<td>SY-2101</td>
<td>Update on dose confirmation study, registration pathway and timing</td>
<td>2H 23</td>
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<tr>
<td>in APL</td>
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2 Evaluate Pharma market estimate includes all risk groups for MDS.
3 Market estimate includes all AML (fit and unfit).
MYELODYSPLASTIC SYNDROME (MDS)
is a bone marrow disorder in which the bone marrow does not produce enough healthy blood cells. MDS is progressive in nature with a poor prognosis. Approved therapies for higher-risk MDS offer limited efficacy, underscoring the need for better treatment options.

ACUTE MYELOID LEUKEMIA (AML)
is very similar to MDS. AML is a cancer of the blood forming cells in the bone marrow. Approximately 1/3 of patients do not respond to the current standard of care, and nearly all relapse with poor prognosis for survival.

We are developing TAMIBAROTENE for the treatment of higher-risk MDS (HR-MDS) and newly diagnosed unfit AML

TAMIBAROTENE (formerly SY-1425) is an oral selective retinoic acid receptor alpha (RARA) agonist that we are developing for genomically defined subsets of patients whose disease is characterized by the overexpression of the RARA gene. Approximately 30% of AML patients and 50% of MDS patients have RARA overexpression.

- 50% of MDS patients are positive for RARA overexpression
- 30% of AML patients are positive for RARA overexpression

ACUTE PROMYELOCYTIC LEUKEMIA (APL)
APL is a unique subtype of AML and is defined by a fusion of the RARA and PML genes. An IV form of arsenic trioxide (ATO) is the current standard of care, but it is very burdensome on the patient, requiring up to 140 infusions over the course of a year.

- Up to 140 infusions x 2-4 hours over nearly a year.

Our Clinical Trials

SELECT-MDS-1 (Phase 3)
Investigating tamibarotene in newly diagnosed HR-MDS patients with RARA overexpression
- Phase 3, randomized, double-blind, placebo-controlled study
- Evaluating tamibarotene in combination with azacitidine, compared with azacitidine alone
- Primary endpoint for potential approval: Complete response (CR) rate - 190 patients
- Key secondary endpoint of Overall Survival (OS) - approximately 550 patients
- Fast Track designation from the FDA

SELECT-AML-1 (Phase 2)
Investigating tamibarotene in newly diagnosed unfit AML patients with RARA overexpression
- Phase 2, randomized study in approximately 80 patients
- Evaluating tamibarotene in combination with venetoclax/azacitidine compared to venetoclax/azacitidine alone
- Primary endpoint for potential approval: Complete response (CR) rate
- Translational data support the potential of our RARA biomarker to enrich not only for patients likely to respond to tamibarotene, but to those potentially resistant to ven/aza

SY-2101 PROGRAM
- Developing a novel oral form of ATO (SY-2101) with an opportunity to replace the standard of care for APL patients
- SY-2101 is being evaluated in a PK and dose confirmation study
- Encouraging early data has demonstrated high oral bioavailability with exposures comparable to IV ATO

Forward Looking Statements
This fact sheet contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995 concerning Syros and other matters, such as Syros’ clinical development plans, including with respect to tamibarotene and SY-2101, Syros’ ability to deliver benefit to patients and value to stockholders, the timing and impact of upcoming clinical data readouts, and the sufficiency of Syros’ capital resources to fund its operating expenses and capital expenditure requirements into 2025. These statements may discuss goals, intentions and expectations as to future plans, trends, results, events or 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 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. 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’ public filings with the U.S. Securities and Exchange Commission. 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.

Footnotes:
1 Patients with MDS: RARA-positivity based on Syros data on file from Study SY-1425-201 and the SELECT-MDS-1 Study (May 27, 2022)
2 Patients with AML: Prevalence of RARA-positive patients based on data presented at ESH 2017 and ESH 2019; FS26 Acute Promyelocytic Leukemia Facts, 2015; NCCN AML treatment guidelines (Nov 2020); Trisenox (arsenic trioxide) USPI