An Expression Makes a World of Difference

September 2022

Forward-looking statements

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 (the Securities Act) concerning Syros, Tyme Technologies (Tyme), the proposed merger transaction with Tyme, and other matters, such as Syros' clinical development plans, including with respect to tamibarotene, SY-2101 and SY-5609, Syros' ability to deliver benefit to patients and value to stockholders, the timing and impact of upcoming clinical and preclinical data readouts, the timing for submitting a new drug application to the Food and Drug Administration, the ability to secure additional capital, and the sufficiency of Syros' capital resources to fund its operating expenses and capital expenditure requirements into the second quarter of 2023 or into 2025 upon the completion of the merger, PIPE and after giving effect to certain provision of the loan agreement amendment. These statements may discuss goals, intentions and expectations as to future plans, trends, events, results of operations or financial condition, or otherwise, based on current beliefs of the management of Syros and Tyme, as well as assumptions made by, and information currently available to, management of Syros and Tyme. 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, 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. Additional factors that could cause actual results to differ materially from those contained in any forward-looking statement include, without limitation, the risk that the conditions to the closing of the proposed transactions are not satisfied, including the failure to obtain stockholder approval for the transactions or to complete the PIPE financing in a timely manner or at all; uncertainties as to the timing of the consummation of the transactions and the ability of each of Syros and Tyme to consummate the transaction, including the PIPE financing; risks related to Tyme's continued listing on the Nasdaq Stock Market until closing of the proposed transactions; risks related to Syros' and Tyme's ability to correctly estimate their respective operating expenses and expenses associated with the transactions, as well as uncertainties regarding the impact any delay in the closing would have on the anticipated cash resources of the combined company upon closing and other events and unanticipated spending and costs that could reduce the combined company's cash resources; the ability of Syros or Tyme to protect their respective intellectual property rights; competitive responses to the transaction; unexpected costs, charges or expenses resulting from the transaction; potential adverse reactions or changes to business relationships resulting from the announcement or completion of the transaction; and legislative, regulatory, political and economic developments. 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, 2021, Syros' Quarterly Report on Form 10-Q for the quarter ended June 30, 2022 and Tyme's Annual Report on Form 10-K for the year ended March 31, 2022, each of which is on file with the Securities and Exchange Commission (SEC). In addition, the extent to which the COVID-19 pandemic continues to impact the proposed transactions 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. Syros and Tyme can give no assurance that the conditions to the transactions will be satisfied. Except as required by applicable law, Syros and Tyme undertake 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.

No Offer or Solicitation
This presentation is not a proxy statement or solicitation of a proxy, consent or authorization with respect to any securities or in respect of the proposed business combination with Tyme and shall not constitute an offer to sell or a solicitation of an offer to buy any securities nor shall there be any sale of securities in any state or jurisdiction in which such offer, solicitation, or sale would be unlawful prior to registration or qualification under the securities laws of any such state or jurisdiction. No offer of securities shall be made except by means of a prospectus meeting the requirements of the Securities Act.

Additional Information and Where to Find It
In connection with the proposed merger transaction with Tyme, Syros filed a Registration Statement on Form S-4 (Registration Statement) with the SEC on July 18, 2022, which was subsequently amended on August 1, 2022. The Registration Statement was declared effective by the SEC on August 8, 2022, and Syros and Tyme commenced mailing of the joint proxy statement/prospectus contained in the Registration Statement to their respective stockholders on or about August 10, 2022. Syros supplemented the joint proxy statement/prospectus with supplemental disclosures included in a Current Report on Form 10-K filed on September 2, 2022. Syros may also file other relevant documents with the SEC regarding the proposed transactions. Investors and security holders are urged to read the Registration Statement and the joint proxy statement/prospectus carefully before making any voting or investment decision with respect to the proposed transactions. The Registration Statement and the joint proxy statement/prospectus contain important information about Syros, Tyme, the transactions and related matters. Investors and security holders may obtain free copies of the Registration Statement and the joint proxy statement/prospectus and other documents filed with the SEC by Syros and Tyme through the web site maintained by the SEC at www.sec.gov. In addition, investors and security holders may obtain free copies of the Registration Statement and the joint proxy statement/prospectus from Syros by contacting hannahd@sternir.com or from Tyme by contacting investorrelations@tymeinc.com.

Participants in the Solicitation
Syros and Tyme, and their respective directors and executive officers, may be deemed to be participants in the solicitation of proxies in respect of the transactions contemplated by the merger agreement. Information regarding Syros' directors and executive officers and Tyme's directors and executive officers, including their interests in the transactions, is contained in the Registration Statement on file with the SEC. These documents can be obtained free of charge from the sources indicated above.

Cash runway extends into 2025

Transaction details:

- Proposed merger with TYME expected to raise proceeds of approximately $60 million
- PIPE commitments of $130 million
- Oxford amendment extends interest only period and maturity date

Transactions are expected to close concurrently in 2H 2022, subject to stockholder approval and other customary conditions

Expected to Raise Total Capital of ~$190 million

Expected capital will allow us to progress our later-stage targeted hematology programs in Phase 3 trials and support commercialization activities:

- SELECT-MDS-1 trial of tamibarotene
- Randomized portion of the SELECT-AML-1 trial of tamibarotene
- Phase 3 trial of SY-2101 in APL

Advancing our diversified clinical pipeline

Program	Indication	Early Clinical	Mid-clinical	Pivotal	Commercial Rights
Tamibarotene (oral RARα agonist)	Newly diagnosed HR-MDS (w/aza)	SELECT-MDS-1 Trial			SYROS Americas, Europe, Australia, Israel & Russia
	Newly diagnosed unfit AML (w/ven+aza)	SELECT-AML-1 Trial			
SY-2101 (oral ATO)	Newly diagnosed APL (w/ATRA)	Dose confirmation study	Ph3 2H 2023		SYROS
SY-5609 (oral CDK7 inhibitor)	Metastatic pancreatic cancer (w/ chemo)	Safety Lead-In			SYROS
	Colorectal cancer (w/atezolizumab)*	Ph1/1b Roche			

Tamibarotene is approved in Japan as Amnolake® for patients with relapsed/refractory APL
*Roche-sponsored trial

Multiple value-driving milestones

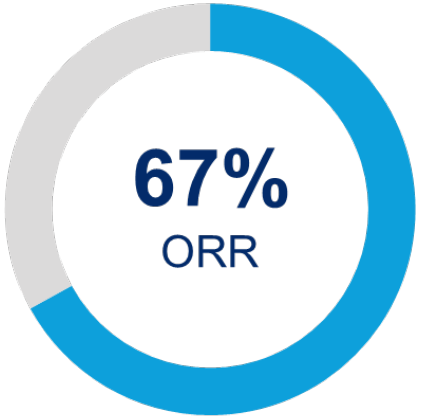
Tamibarotene in HR-MDS	Pivotal data from SELECT-MDS-1 Phase 3 trial	**4Q23/1Q24**
	Potential NDA filing	**2024**
Tamibarotene in AML	Clinical activity data from safety lead-in SELECT-AML-1 trial	**2H 2022**
	Data from randomized SELECT-AML-1 trial	**2023/2024**
SY-2101 in APL	PK and safety data	✓
	Initiation of Phase 3 trial	**2H 2023**
SY-5609	Clinical activity data from safety lead-in in pancreatic cancer	**2H 2022**
Discovery	Development candidate named from CDK12 program	✓

Tamibarotene
Selective oral RARα agonist

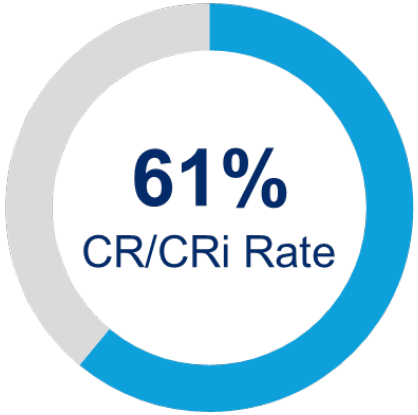
Value of Tamibarotene

- Selective and potent RARα agonist; ~50% of MDS patients and ~30% of AML patients are RARA-positive
- RARA biomarker discovered from Syros' gene control discovery engine
- Ongoing Phase 3 trial in newly diagnosed HR-MDS, potentially the first therapy for a targeted population in HR-MDS with broad potential in RARA-positive patients
- Oral drug with novel mechanism and favorable tolerability profile supports use in combination and in front-line treatment for those unfit to receive chemotherapy
- Targeting a multi-billion-dollar opportunity in HR-MDS and AML

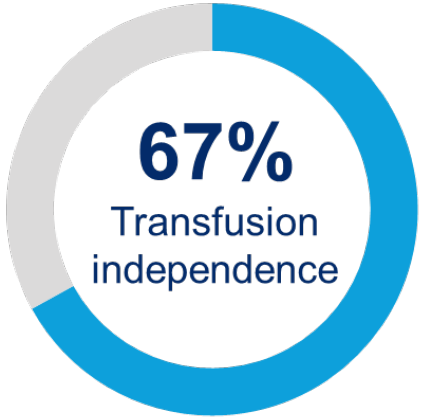
High CR rates, rapid onset of action, and clinically meaningful durability in Phase 2 trial in RARA-positive newly diagnosed unfit AML



1.2 months
Time to response



10.8 months
Duration of response

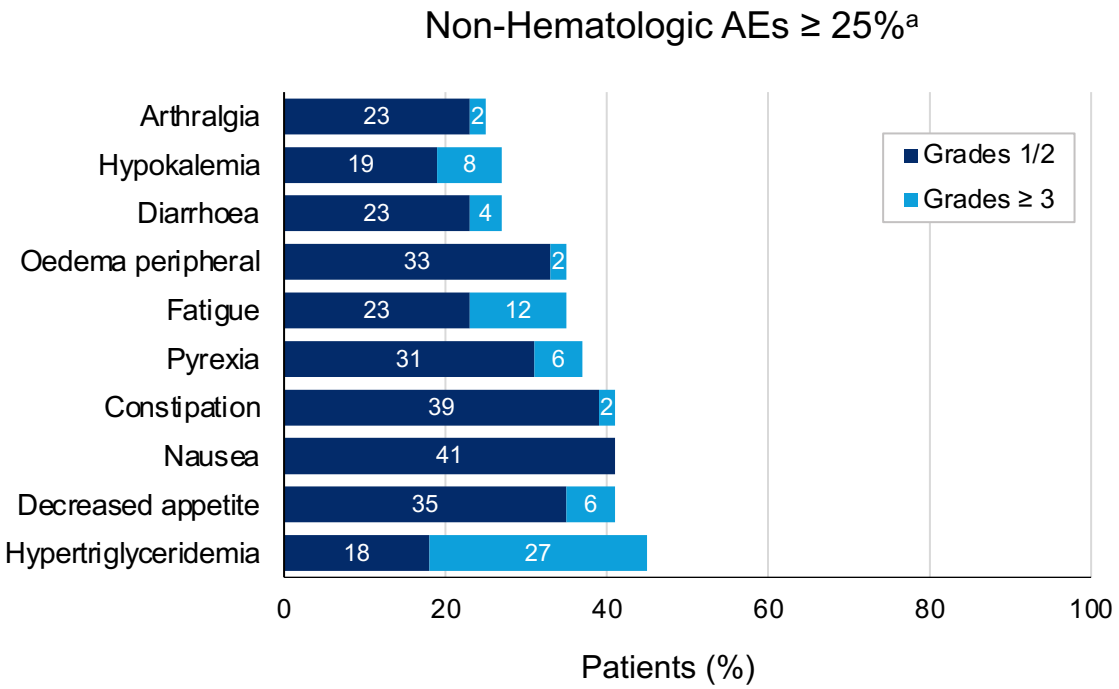


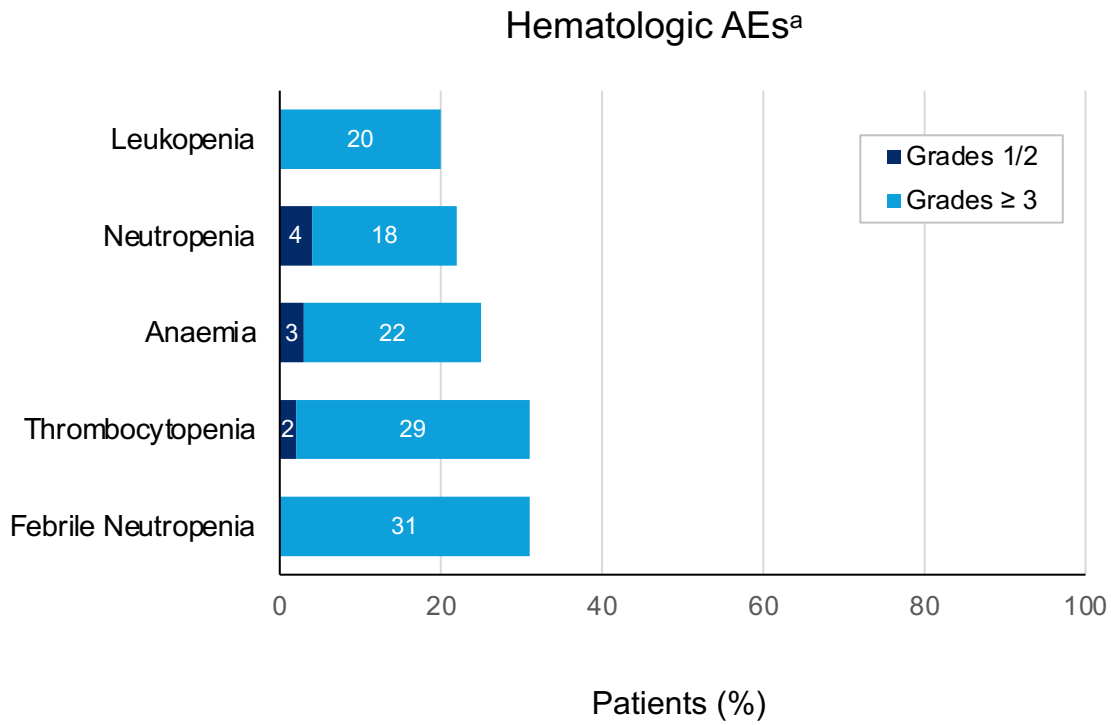
18 months
Overall survival for complete responders

- 89% of CRs were deep molecular or cytogenetic CRs
- Responses seen irrespective of mutation or cytogenetic risk
- Response rates in RARA-negative patients comparable to historical rates for single-agent aza[1-3]
- 67% of low blast count AML patients achieved CR with tamibarotene/aza
  - 27% of RARA-negative low blast count AML patients achieved CR

Data from 18 response evaluable RARA-positive and 28 response evaluable RARA-negative patients presented at ASH 2020 meeting
Data from 6 response-evaluable RARA+ low blast count AML patients and 11 response evaluable RARA-negative low blast count AML patients presented at ASH 2020 meeting
[1]Dombret, Blood 2015; [2]Fenaux, JCO 2010; [3]Thepot, American Journal of Hematology 2014

Safety profile supports multiple combinations and long-term use, enhancing opportunity

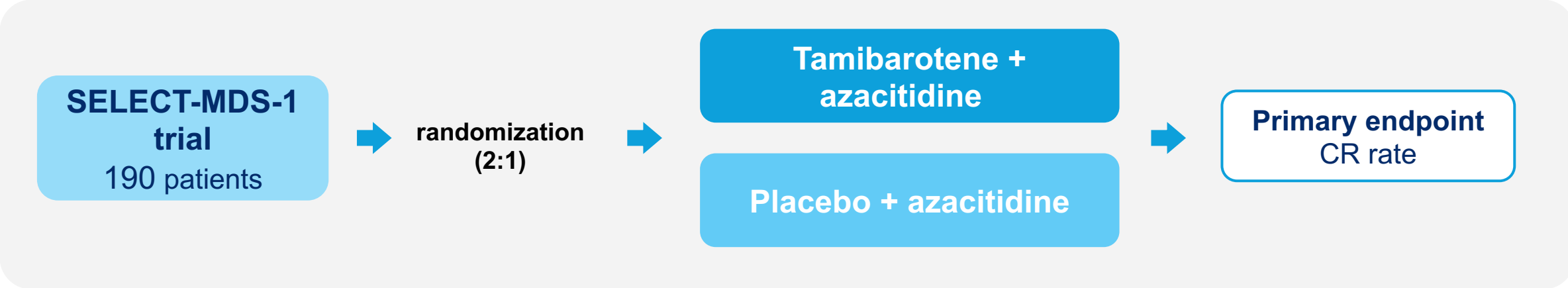




- Generally well-tolerated combination in ND unfit AML patients
- No increase in neutropenia, anemia and thrombocytopenia compared to single-agent aza
- Majority of non-hematologic AEs are low grade and reversible

[a]Includes all enrolled ND unfit patients, N=51.
Data presented at ASH 2020 meeting

Ongoing SELECT-MDS-1 Phase 3 trial in RARA-positive newly diagnosed HR-MDS



- Robustly designed, double-blind, placebo-controlled study
- 90% power to detect a difference in CR rates between experimental and control arms
- 2:1 randomization with one-sided alpha of 0.025
- FDA feedback supports:
  - Focus on RARA+ population
  - CR as primary endpoint for approval
  - Azacitidine as appropriate comparator

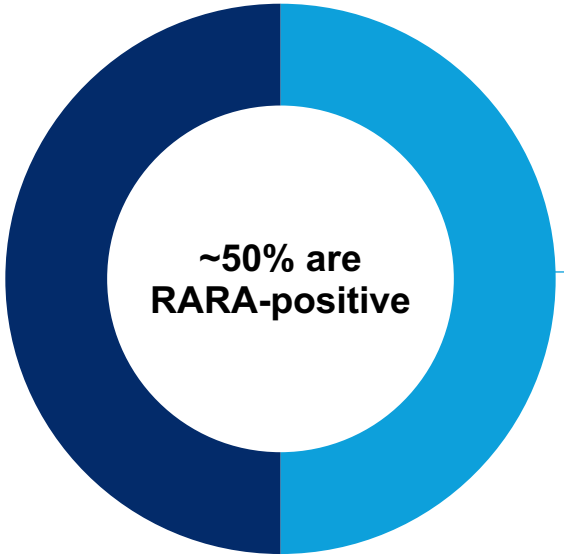
Key Milestones

Phase 3 data	4Q23/1Q24
Potential NDA filing	2024

SYROS

Tamibarotene has the potential to set a new treatment paradigm for RARA-positive HR-MDS patients

~21,000 newly diagnosed HR-MDS patients in US and EU estimated annually



COMPETITIVE LANDSCAPE OF APPROVED THERAPIES

Targeted Population	All Comers Population
N/A	Azacitidine or decitabine - offers limited efficacy

Syros' Product Candidate

RARA+

Tamibarotene + aza

Targets ~50% of patients

Physicians are familiar with companion diagnostics to determine optimal treatment for AML → Anticipate rapid adaption of targeted therapy in HR-MDS

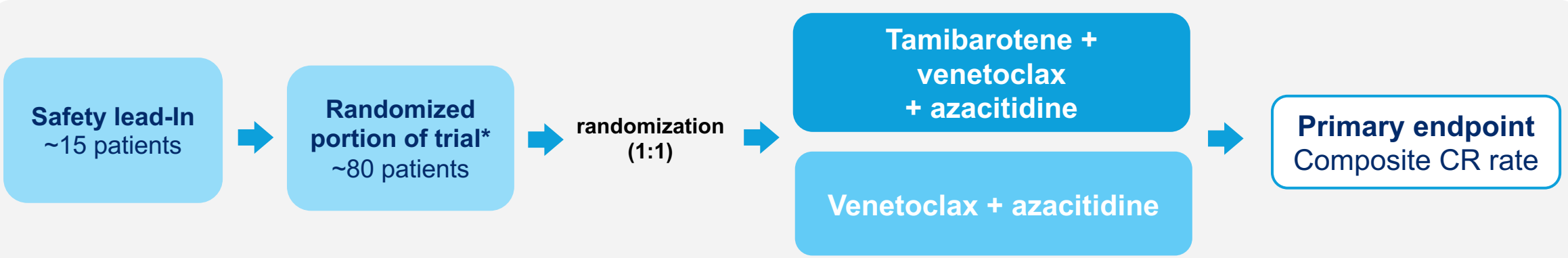
MDS represents a ~$3.3B* market by 2026

Syros is developing potentially the first therapy for a targeted population in HR-MDS

NOTE:
RARA-positivity based on Syros data on file from Study SY-1425-201 and the SELECT-MDS-1 Study (27May2022) from over 175 patients with MDS
Sources: Decision Resources Group, NCCN guidelines,
*Evaluate Pharma market estimate includes all risk groups for MDS

SYROS

Ongoing SELECT-AML-1 Phase 2 trial of triplet regimen (Tami/Ven/Aza) in ND RARA-positive unfit AML patients



- Also evaluating triplet as salvage strategy for patients in control arm who do not respond to ven/aza

Translational data support potential for RARA biomarker to enrich for patients more likely to respond to tamibarotene, for whom the standard of care is suboptimal

- 30% of patients do not respond to upfront treatment with ven/aza and a majority of those with initial response ultimately relapse
- Venetoclax resistance is associated with monocytic phenotype [1-3]; most RARA-positive patients, including those who achieved CR/CRi in tamibarotene trial, have this monocytic phenotype[4]

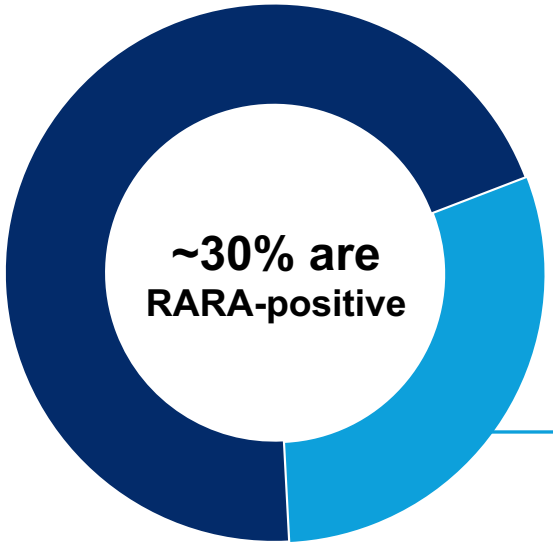
Key Milestones

Safety lead-in data	2H 2022
Randomized data	2023/2024

[1]Zhang, Nature 2018; [2]Kuusanmäki, Haematologica 2019; [3]Pei, Cancer Discovery 2020; [4]Fiore, ASH 2020

Tamibarotene targets RARA-positive patients which represents one of the largest targeted populations in unfit AML

~25,000 Newly Diagnosed Unfit AML Patients in US and EU



COMPETITIVE LANDSCAPE OF APPROVED THERAPIES

Targeted Populations

FLT3+

IDH1+

IDH2+

XOSPATA® (r/r)

TIBSOVO ®

IDHIFA®

Targets ~30% of patients

Targets ~8% of patients

Targets ~11% of patients

Syros' Product Candidate

RARA+

Tamibarotene + ven/aza

Targets ~30% of patients

All Comers Populations

HMA[1] + venetoclax

LDAC + glasdegib

~1/3 of patients do not respond to standard of care ven/aza and majority of those with initial response ultimately relapse.

Newly diagnosed AML represents a ~$6.6 billion* market by 2025

Epidemiology: DRG. Market sizing: Evaluate Pharma NOTE*: market estimate includes all AML (fit and unfit)

Prevalence of RARA-positive patients based on data presented at ESH 2017 and ESH 2019; Resistant Ven population - Dinardo, NEJM 2020; Dinardo, Blood 2019
Prevalence and Clinical Effect of IDH1 and IDH2 Mutations Among Cytogenetically Normal Acute Myeloid Leukemia Patients, Clin Lymphoma Myeloma Leuk. 2015 Sep;15(9):550-5.
Daver N, Schlenk RF, Russell NH, et al. Targeting FLT3 mutations in AML: review of current knowledge and evidence. Leukemia. 2019;33(2):299–312.

SY-2101
Novel oral form of arsenic trioxide

Value of SY-2101

- Novel oral form of arsenic trioxide (ATO) with opportunity to replace standard of care for APL patients; APL is approximately 10% of all AML patients
- Orally bioavailable with exposures consistent with IV ATO
- Clear development path to approval in front-line APL
- Potential for rapid adoption in front-line APL, including specialized commercial effort and synergies with tamibarotene

Clear development path in front-line APL

- Based on preliminary data as of July 2022 from dose confirmation study:
  The first cross-over data directly comparing SY-2101 to the approved dose of IV ATO
  - SY-2101 administered at 15 mg achieved exposures comparable to IV ATO administered at 0.15 mg/kg based on Cmax and AUC parameters
  - SY-2101 showed high oral bioavailability of ~80%
  - Continues to support favorable tolerability and safety profile
- FDA feedback from November 2021 supports:
  - Molecular CR as primary endpoint compared to historic data for accelerated approval
  - Event free survival (EFS) as primary endpoint compared to historic data for full approval
  - IV ATO arm for safety comparison
- In July 2022, received feedback from EMA, which together with prior FDA feedback, informs decision to move forward with single registration trial that could support approval of 2101 in the US and EU

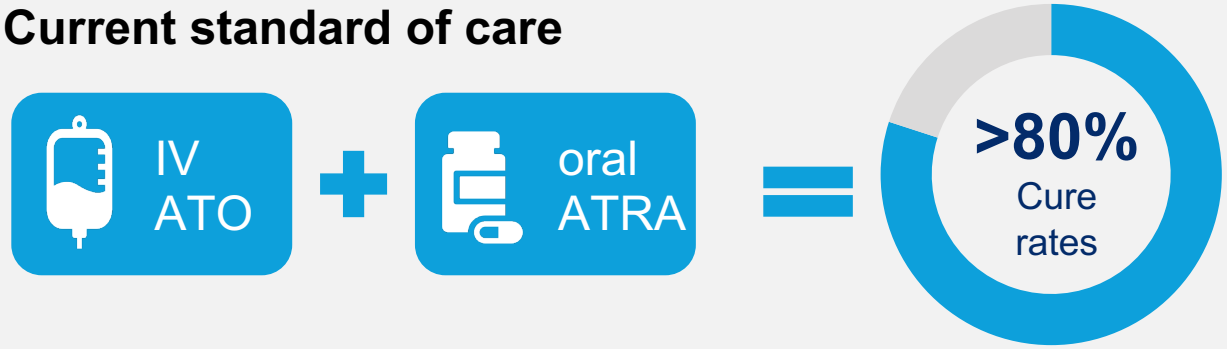
Key Milestones

Initiation of Phase 3 trial	2H 2023

SYROS

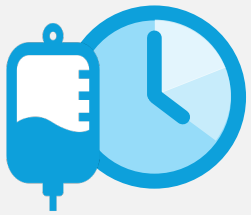
SY-2101 offers significant opportunity to reduce treatment burden, increase access, reduce health care costs and utilization

Current standard of care



Treatment burden:
Current course of treatment involves infusions of

up to 140 x 2-4 hrs



over nearly a year

Market opportunity for an oral therapy:

APL accounts for **~10%** of all adult AML cases diagnosed in US and Europe annually

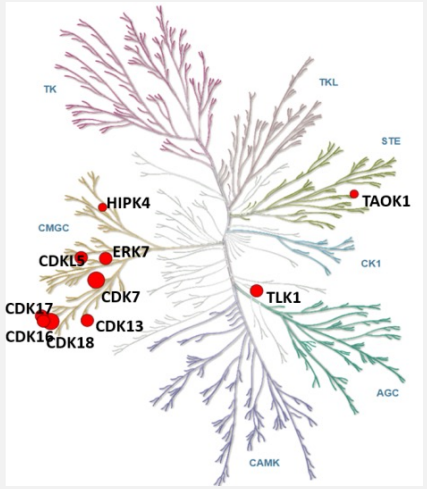
~2,000 patients are diagnosed with APL in the US and EU annually

NCCN AML treatment guidelines (Nov 2020)
Trisenox (arsenic trioxide) USPI

SY-5609
Highly selective and potent oral CDK7 inhibitor

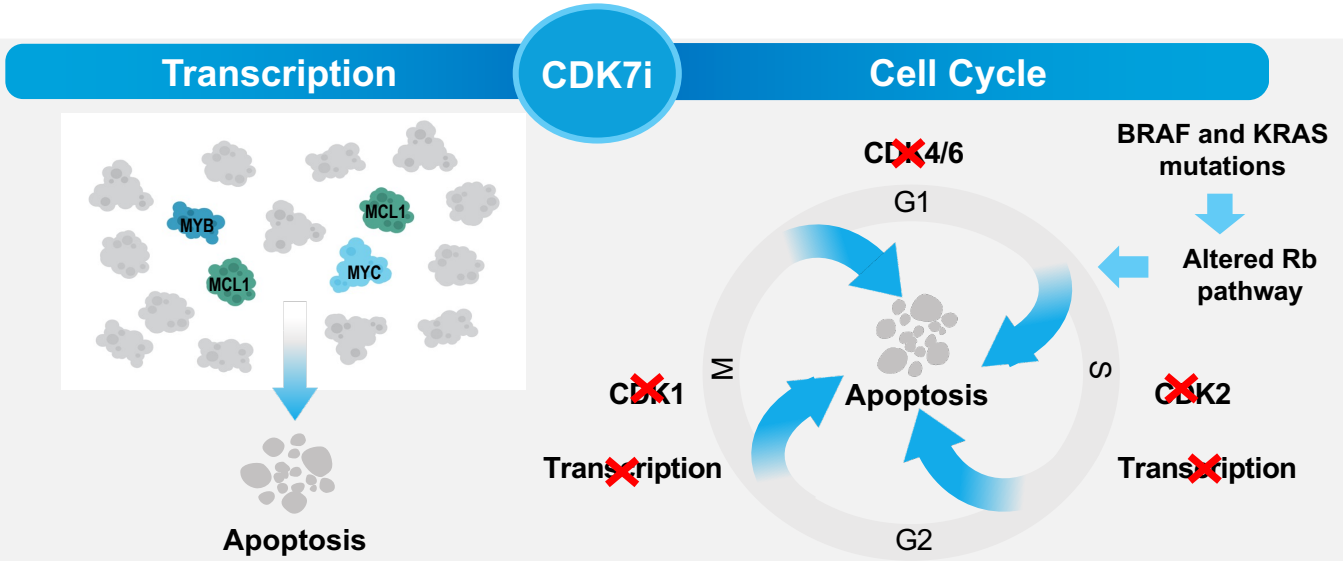
SY-5609: Highly selective and potent oral CDK7 inhibitor

- Strong pre-clinical data support potential across a range of difficult-to-treat solid tumors
- Demonstrated proof of activity and proof of mechanism in refractory solid tumor patients with a generally favorable tolerability profile. Preclinical/clinical data of CDK7 inhibition support plans in PDAC and CRC
- Further validates Syros' gene control discovery engine



- 100-91% Inhibition
- 90-80% Inhibition
- 79-71% Inhibition

SY-5609 is highly selective with subnanomolar potency[1]



[1]Marineau JJ et al, 2021, Discovery of SY-5609: A Selective, Noncovalent Inhibitor of CDK7, J Med Chem
Data presented in October 2019 at EORTC-NCI-AACR Conference

Phase 1 dose escalation study: Favorable tolerability profile with predominantly low-grade AEs

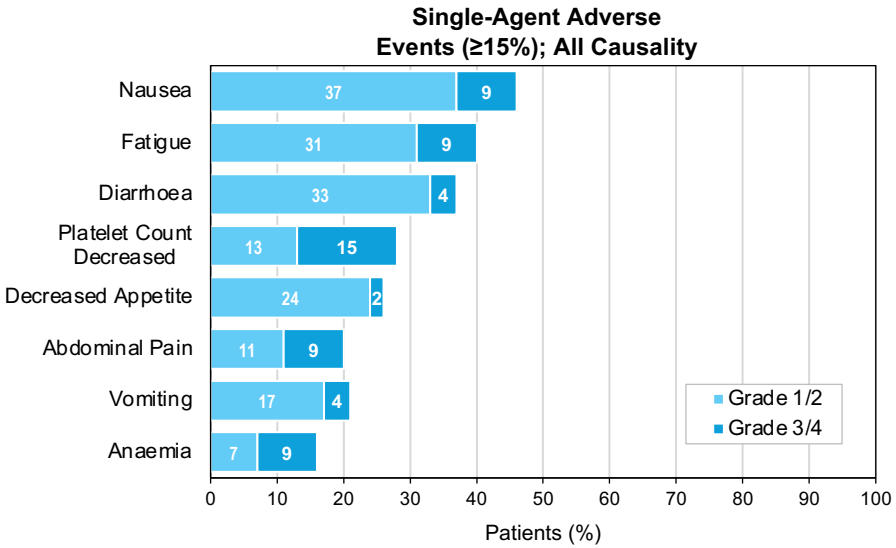
Patient Population

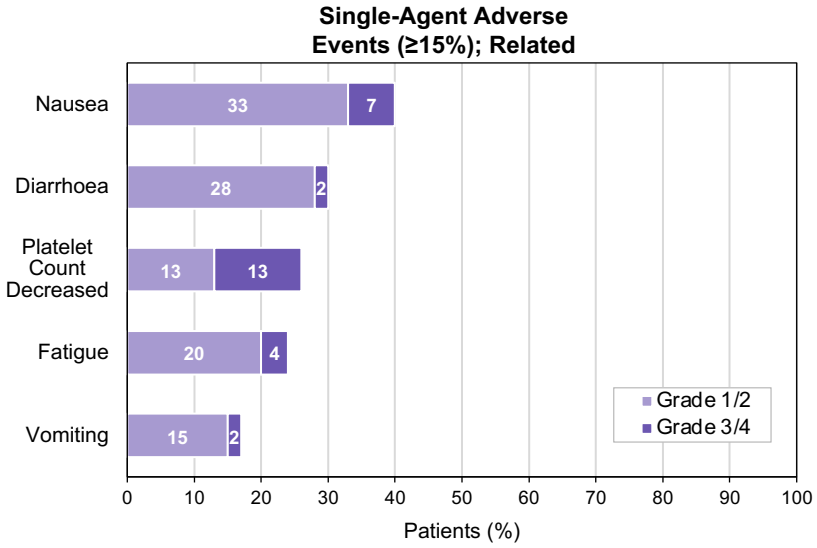
Enrolled patients with advanced breast, colorectal, lung, ovarian or pancreatic cancer, as well as other tumor types with Rb pathway alterations; heavily pretreated with as many as eight prior therapies and a median of four prior therapies

Objectives

Safety, tolerability, PK, PD (POLR2A), antitumor activity

Tolerability was optimized with 7d on/7d off dosing schedule





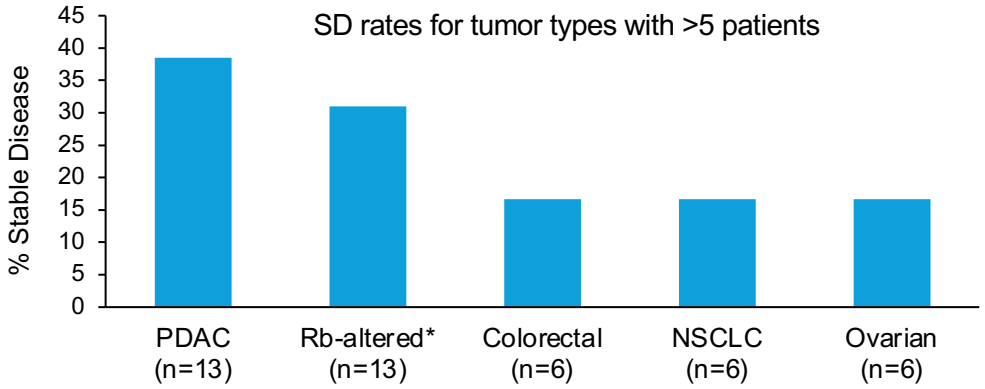
- Manageable safety profile with majority of AEs low-grade and reversible
- Low rate of discontinuation due to AEs at ~7%
- MTD not yet reached at 7d on/7d off with dosing up to 6 mg
- Induction of PD marker in patients treated at 3 mg and above reached levels associated with tumor regressions in preclinical models and with target lesion reductions in study

SYROS

Data presented at ESMO 2021; data cutoff July 6, 2021

Clinical activity seen in heavily pretreated patients; strongest in PDAC, Rb-altered and KRAS-mutant cancers

Highest rates of activity seen in pancreatic cancer patients and Rb-altered tumor cohort[1]



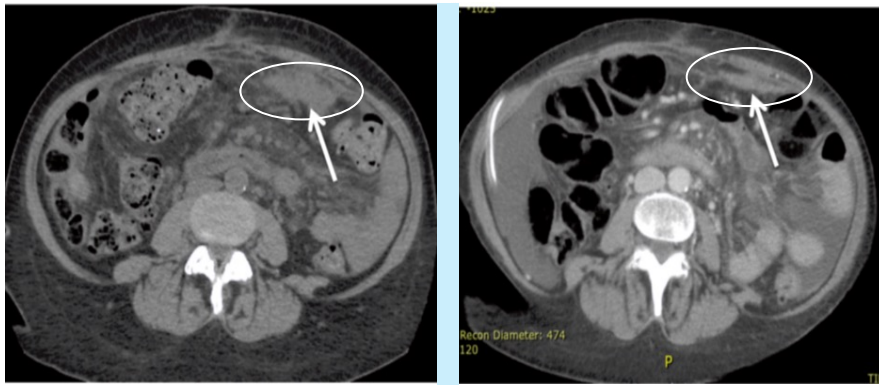
*Rb-altered patients had tumor types other than breast, ovarian, CRC, lung or pancreatic cancer, who were enrolled based on historical molecular evidence of mutation/deletion in Rb pathway gene(s).

- 13 of 45 (28.9%) of response evaluable patients achieved stable disease (SD), 6 had tumor regressions of up to 20%
- 5 of 13 (38.5%) of response-evaluable PDAC patients achieved SD, 2 with tumor shrinkage
  - 3 of 4 PDAC pancreatic cancer patients with serial CA-19-9 data had decreases (32-72%) in this clinically relevant tumor marker
- 58% of the SD patients with mutation data had KRAS mutations compared to 32% with PD
  - 67% of patients with SD who also had tumor shrinkage had KRAS mutations

Heavily pretreated pancreatic cancer patient in 3rd relapse achieve durable SD and significant tumor marker reduction of 72%

- Scan showed 20% decrease in target lesion
- Remained in SD for 10 months
- Received 3mg/day on 7d on/7d off schedule for 7+ months on treatment

CT scans show 20% decrease in target lesion



Courtesy, START San Antonio

Data presented at ESMO 2021
[1]Internal company data

Exploring SY-5609 in two distinct approaches based on mechanistic rationale, preclinical data and clinical signals

Pancreatic Cancer

- KRAS mutations are ubiquitous and powerful activators of cell signaling and transcriptional programs
- Compelling preclinical data and synergy with gemcitabine
- Single agent SY-5609 showed:
  - Clinical activity in relapsed refractory pancreatic cancer and Rb-altered tumors
  - KRAS mutations associated with clinical activity

BRAF-mutant Colorectal Cancer

- BRAF mutations, present in 10% of colorectal cancer patients, are powerful activators of cell signaling and transcriptional programs
- Compelling preclinical data as single agent
- CDK7 inhibition enhances anti-tumor activity of immunotherapy in preclinical models

Ongoing safety lead-in portion of the Phase 1 trial in relapsed pancreatic patients

Patient population
Metastatic patients who have progressed following first-line treatment with FOLFIRINOX

Doublet with gemcitabine

Safety lead-in

Triplet with gemcitabine and nab-paclitaxel

Safety lead-in

Safety lead-in portion of the trial will be evaluating:
- Safety
- Tolerability
- Signs of clinical activity

- SY-5609 administered 7d on/7d off, at a starting dose of 4 mg
- Gemcitabine and nab-paclitaxel administered at approved doses

High unmet need in metastatic pancreatic cancer

- Incidence of second-line patients is ~27,500 in US[1]
- Only approved second-line therapy (Onivyde® + 5-FU/LV) has PFS of 3.1 months[2]

Key Milestones

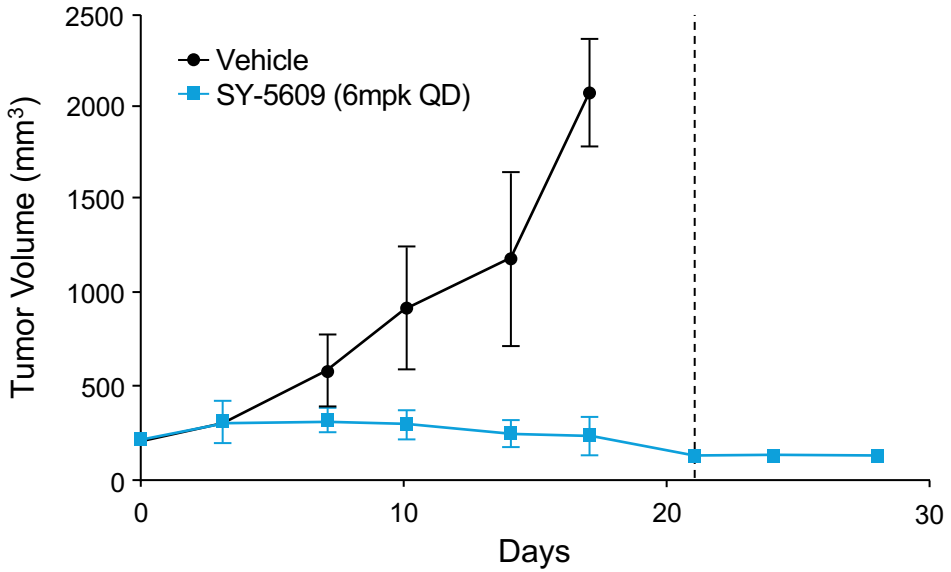
Safety lead-in data	2H 2022

[1]Sadhu and Vinuesa, Pancreatic Cancer Disease Landscape & Forecast, DRG, 2021.; [2]Wang-Gillam et al, 2015.;

Preclinical data support SY-5609 in BRAF-mutant CRC in combination with PDL1 inhibitor: SY-5609 part of Roche's Phase 1/1b INTRINSIC trial

First clinical investigation of CDK7 inhibitor with an immunotherapy

Robust anti-tumor activity in BRAF-mutant CRC as single agent



- 67% (20/30) of models demonstrated ≥ 50% TGI
- 23% (7/30) demonstrated deep responses of ≥ 90% TGI
- Deep responses enriched in BRAF-mutant (5/10) models

Key Milestones:

- Roche is now actively enrolling patients in the arm of its ongoing Phase 1/1b INTRINISIC trial evaluating SY-5609 in combination with atezolizumab
  - Roche is the sponsor of the trial and Syros is supplying SY-5609

CDK7 inhibition enhances anti-tumor activity of PD-1 inhibition[1]

- CDK7 inhibitor induces DNA replication stress and genome instability in cancer cells, triggering immune-response signaling
- In animal models, CDK7 inhibitor enhances tumor response to anti-PD1 immunotherapy
  - Prolonging overall survival, and increasing immune cell infiltrates

CRC data presented in May 2020 at ASCO Virtual Symposium.

1. Zhang et al., 2020, Cancer Cell 37, 1-18

Gene Control Discovery Engine

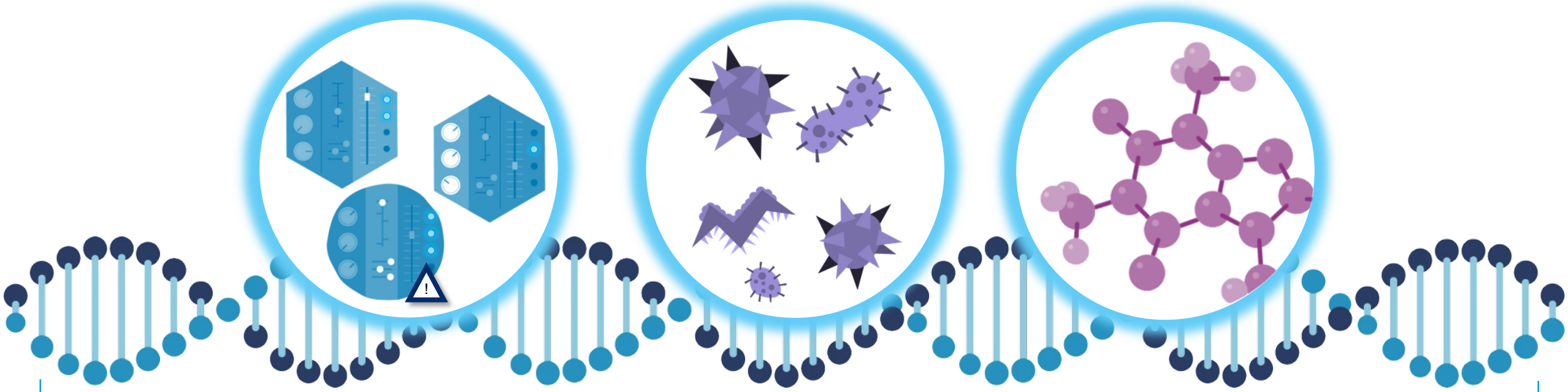
SYROS

Redefining the power of small molecules to control expression of genes

Regulatory Genomics

Disease Biology

Transcriptional Chemistry



98% Previously unexplored regulatory regions of the genome control expression of genes determining cell function; majority of disease variation found in these regions

Patient Impact

Medicines that control the expression of genes to provide profound benefit for patients with severe diseases

SYROS

Seeking partnerships for our oncology discovery programs

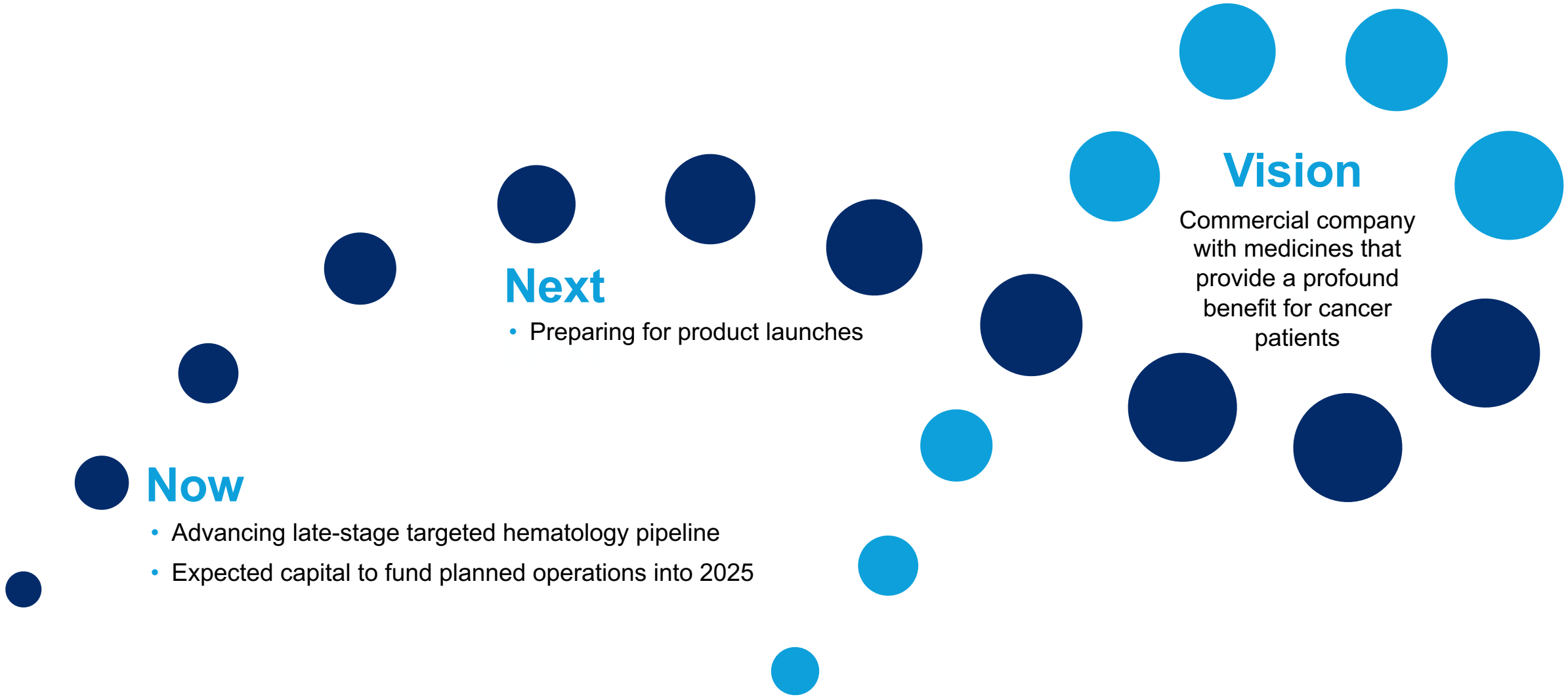
ONCOLOGY

Program	Target Development	Drug Discovery	IND-enabling	Commercial Rights
CDK12 inhibitor				SYROS
CDK11 inhibitor				SYROS
WRN inhibitor				SYROS

PARTNERED PROGRAMS

Program	Target Development	Drug Discovery	IND-enabling	Commercial Rights
Sickle cell disease & beta thalassemia				GBT Syros US co-promote option
Myeloproliferative neoplasms				Incyte

Rapidly advancing toward our vision



Now

- Advancing late-stage targeted hematology pipeline
- Expected capital to fund planned operations into 2025

Next

- Preparing for product launches

Vision

Commercial company with medicines that provide a profound benefit for cancer patients

Appendix

Preclinical data support SY-5609 in relapsed pancreatic cancer patients in combination with chemotherapy

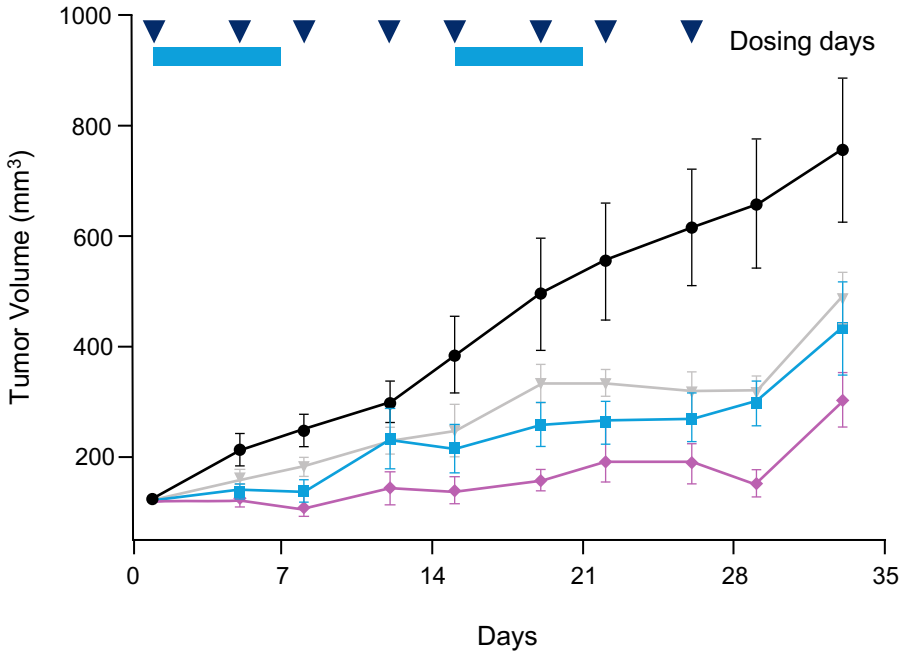
SY-5609 induced regressions in KRAS-mutant models, including those derived from heavily pretreated patients

Model ID	TGI (%)	Prior treatments	KRAS mutation
1	>100	0	G12D
2	>100	3	NRAS
3	>100	5	G12D
4	>100	3	G12D
5	92	0	G12V
6	87	0	G12V
7	42	4	G12D
8	8	0	G12R

Dosed at 6mg/kg QD for 21 days

- Regressions seen in 50% (4/8) models
  - 3/4 models with regressions derived from heavily pretreated patients

SY-5609 potentiated activity of gemcitibine in pancreatic cancer model using 7d on/7d off regimen




SYROS