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): December 2, 2019

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 **Cambridge, Massachusetts**	**02140**
(Address of Principal Executive Offices)	**(Zip Code)**

Registrant's telephone number, including area code: (617) 744-1340

620 Memorial Drive, Cambridge, Massachusetts 02139
(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 (*see* General Instruction A.2. below):

☐ 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 or to be 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, $0.001 par value	**SYRS**	**Nasdaq Global Select 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, we intend to conduct meetings with third parties in which our current corporate slide presentation is presented. A copy of this slide presentation, dated December 2, 2019, 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 9.01 Financial Statements and Exhibits.

Exhibit No.	Description
99.1	Slide presentation dated December 2, 2019

SIGNATURE

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: December 2, 2019

By: /s/ Gerald E. Quirk
Gerald E. Quirk
Chief Legal & Administrative Officer

Exhibit 99.1

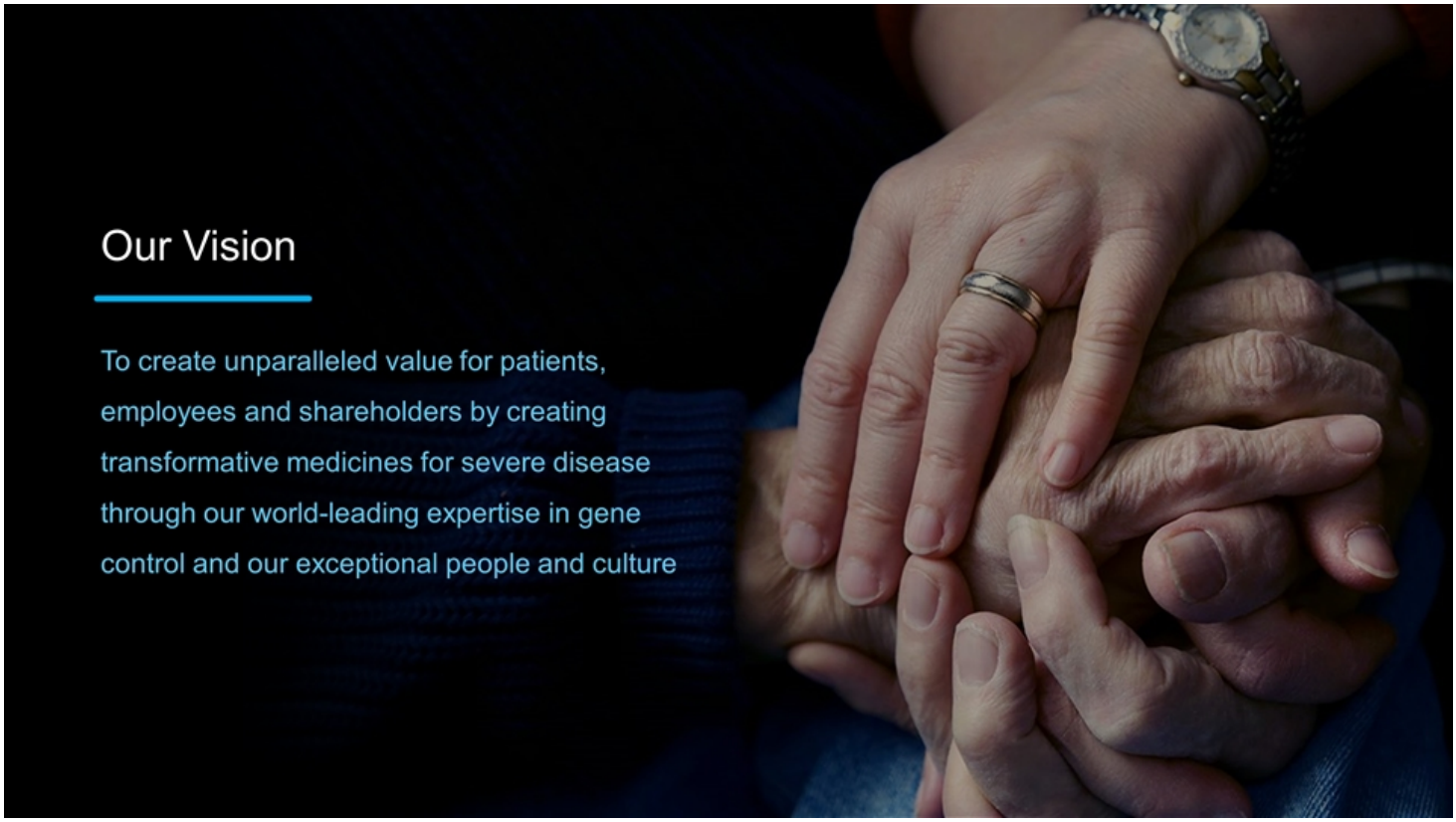

SYROS
An Expression Makes a World of Difference
December 2, 2019

Forward-looking statements

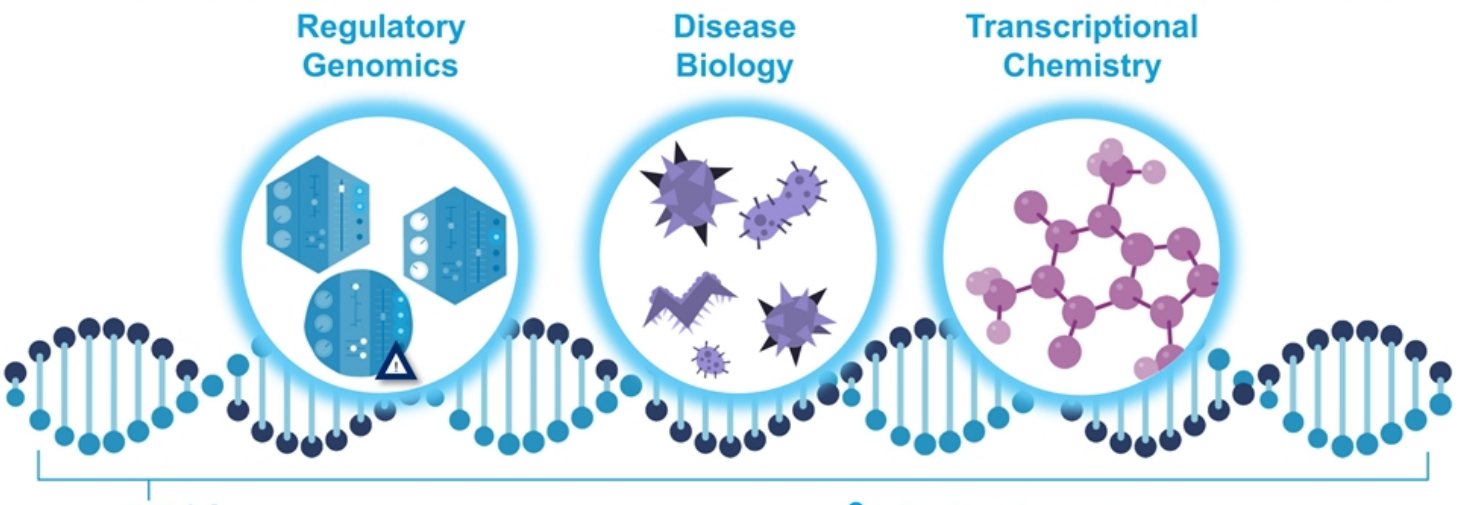
This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this presentation, including statements regarding our strategy, research and clinical development plans, collaborations, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “plan,” “predict,” “project,” “target,” “potential,” “will,” “would,” “could,” “should,” “continue,” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. 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 whether or when Incyte will exercise any of its options or any option exercise fees, milestone payments or royalties under the Incyte collaboration will ever be paid, our ability to: advance the development of our programs, including SY-1425 and SY-5609, under the timelines we project in current and future clinical trials or to achieve clinical proof of concept of SY-1425; demonstrate in any current and future clinical trials the requisite safety, efficacy and combinability of our drug candidates; successfully progress SY-5609 through IND-enabling preclinical studies by the end of 2019 and initiate clinical development in the first quarter of 2020; replicate scientific and non-clinical data in clinical trials; successfully develop a companion diagnostic test to identify patients with the RARA biomarker; obtain and maintain patent protection for our drug candidates and the freedom to operate under third party intellectual property; avail ourselves of accelerated regulatory pathways or obtain and maintain necessary regulatory approvals; identify, enter into and maintain collaboration agreements with third parties, including our ability to perform under the collaboration agreement with Incyte; manage competition; manage expenses; raise the substantial additional capital needed to achieve our business objectives; attract and retain qualified personnel; and successfully execute on our business strategies and long-term vision; risks described under the caption “Risk Factors” in our Annual Report on Form 10-K for the year ended December 31, 2018 and our Quarterly Report on Form 10-Q for the quarter ended September 30, 2019, each of which is on file with the Securities and Exchange Commission (SEC); and risks described in other filings that we may make with the SEC in the future.

Any forward-looking statements contained in this presentation speak only as of the date this presentation is made, and we expressly disclaim any obligation to update any forward-looking statements, whether because of new information, future events or otherwise.


Our Vision
To create unparalleled value for patients, employees and shareholders by creating transformative medicines for severe disease through our world-leading expertise in gene control and our exceptional people and culture

Redefining the power of small molecules to control expression of genes



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

Deep gene control pipeline

Program	Indication	Drug Discovery	IND-Enabling	Early Clinical	Mid-Clinical	Pivotal
SY-1425 (RARα agonist)	Newly diagnosed unfit AML				●	
	R/R AML				●	
SY-5609 (Oral CDK7 inhibitor)	Cancer			●		
CDK12/13 inhibitor	Cancer	●				
Macrophage target	Cancer	●				
Monogenic disease	Sickle cell disease	●				

SY-1425 is approved in Japan as Amnolake® (tamibarotene) for patients with relapsed/refractory APL

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Our vision for SY-1425 in RARA-positive patients

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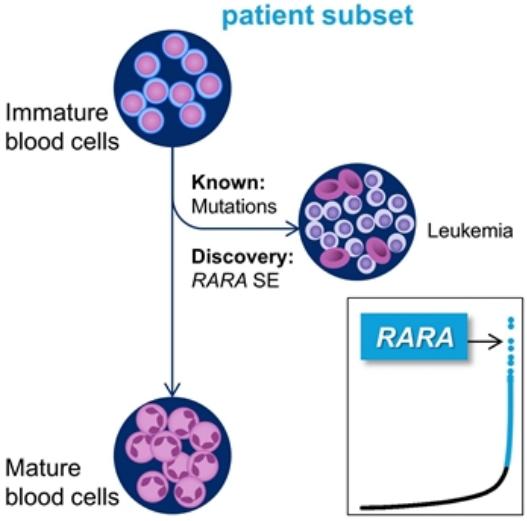
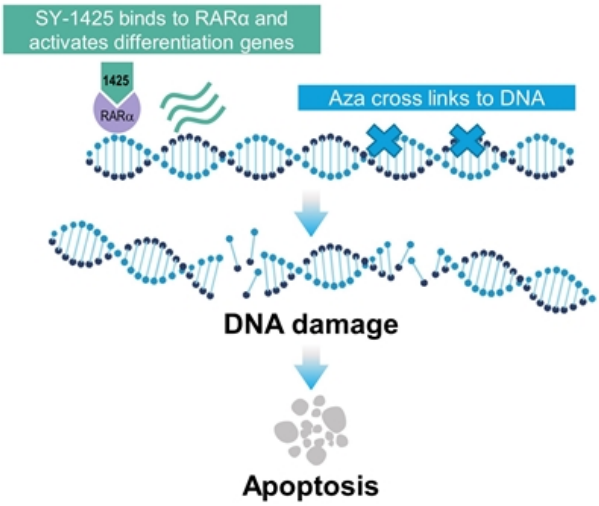
Novel combination approach for RARA-positive AML patients

Gene control platform identifies novel patient subset



SY-1425 enhances apoptosis preclinically



SY-1425 shows synergy with a range of AML therapies in preclinical studies

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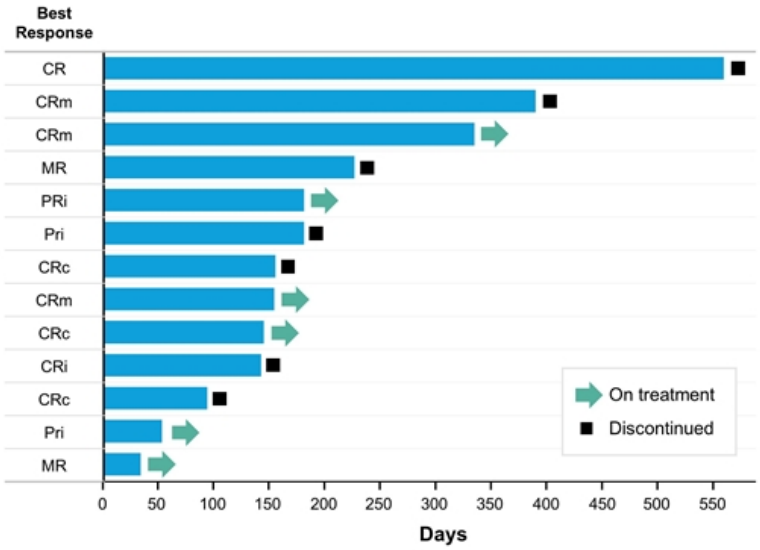
Data published in October 2017 in Cancer Discovery

Data published in October 2018 in Haematologica

SY-1425 in combination with azacitidine shows high complete response rates, deep CRs and rapid onset of action in RARA-positive AML patients



62%
CR/CRi Rate (n=13)

54%
CR Rate (n=13)

82%
Transfusion independence (n=11)

1 month
Time to response

86% of CRs were deep molecular or cytogenetic CRs
Duration of response up to 344 days, with three CRs lasting more than seven months as of data cut-off

SY-1425 in combination with azacitidine has been generally well-tolerated with no evidence of increased toxicities

Preferred Term	All Grades N = 40 n (%)	≥ Grade 3 N = 40 n (%)
Patients with an AE	40 (100)	29 (73)
Hematologic		
Thrombocytopenia	11 (28)	10 (25)
Anemia	9 (23)	9 (23)
Febrile neutropenia	9 (23)	9 (23)

Preferred Term	All Grades N = 40 n (%)	≥ Grade 3 N = 40 n (%)
Patients with an AE	40 (100)	29 (73)
Non-Hematologic		
Nausea	15 (38)	0 (0)
Decreased appetite	15 (38)	3 (8)
Constipation	13 (33)	0 (0)
Fatigue	13 (33)	5 (13)
Edema peripheral	12 (30)	0 (0)
Diarrhea	11 (28)	1 (3)
Pyrexia	11 (28)	2 (5)
Hypertriglyceridemia	11 (28)	6 (15)
Dizziness	10 (25)	0 (0)
Arthralgia	9 (23)	1 (3)
Dyspnea	9 (23)	2 (5)
Dry skin	9 (23)	0 (0)
Rash	9 (23)	1 (3)
Pruritus	8 (20)	0 (0)

- AEs consistent with single-agent SY-1425 or azacitidine in AML
- Rates of myelosuppression comparable to reports of single-agent azacitidine
- Majority of non-hematologic AEs were low grade

Data published in October 2019 at ESH

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Deep CRs and high CR rates in RARA-positive patients support RARA as the optimal biomarker for patient selection

Best IWG Response	RARA Positive n (%)	RARA Negative n (%)
Response Evaluable	13	22
ORR	8 (62)	8 (36)
CR/CRi	8 (62)	6 (27)
CR	7 (54)	3 (14)
CRm	3 (23)	0 (0)
CRc	3 (23)	3 (14)
CRi	1 (8)	3 (14)

- 27% CR/CRi rate in RARA-negative consistent with single-agent azacitidine[1]
- RARA is not a prognostic biomarker in AML, based on analyses of TCGA, BeatAML and company data
- RARA does not appear to enrich for genes that may be associated with responsiveness to azacitidine

SYROS

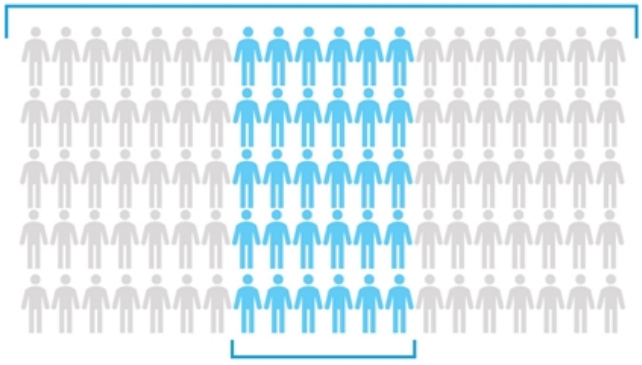
Data published in October 2019 at ESH

[1] Fenaux et al, *JCO* 2010; Dombret et al, *Blood* 2015; Vidaza® (azacitidine) Prescribing Information, Celgene Revision 09/2018.

Significant need for well-tolerated oral therapies that improve outcomes and quality of life

Fast-growing AML market is projected to be ~ $1 billion this year

~30,000 AML patients in US and EU5



~30%
RARA-positive

R/R AML

- Clinical trials are preferred treatment strategy
- Recently approved therapies target limited patient subsets, with composite CR rates in 20-35% range and duration of 4-8 months
- Survival remains low at < 6 months

Newly diagnosed AML

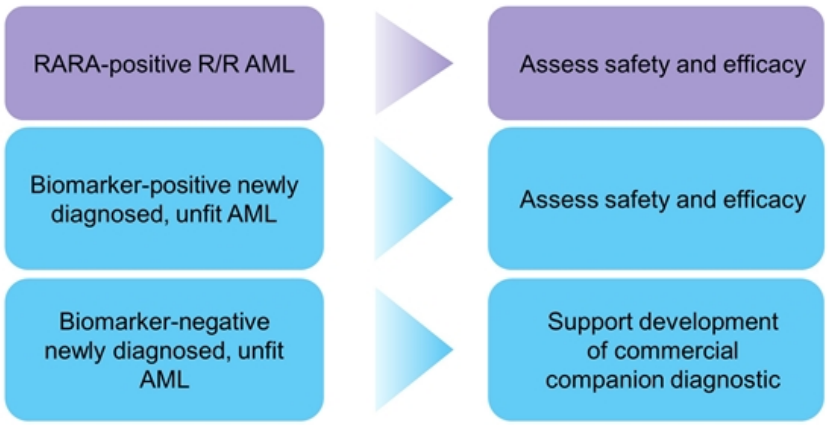
- >50% newly diagnosed patients are elderly/unfit
- Combinations emerging as standard-of-care
  - Despite high CR rates, duration of response limited

*2018 incidence in the U.S. and the EU 5 (UK, Germany, France, Spain and Italy) from Decision Resources Group. Annual sales forecast from Decision Resources Group.
Sources: NCCN guidelines AML (Feb 2018); Clinical Lymphoma, Myeloma & Leukemia, 16:625-36 (2016); Blood 120:2454-2465 (2012); Ivosidenib, enasidenib & gilteritinib USPIs.
** Based on data from 201 evaluable patients screened in our ongoing Phase 2 clinical trial of SY-1425

Ongoing Phase 2 trial evaluating SY-1425 in combination with azacitidine in RARA-positive AML, with opportunity for rapid proof-of-concept

- Enrollment complete in newly diagnosed unfit cohorts
- Potential proof-of-concept data in relapsed or refractory AML expected in 2020

Phase 2 clinical trial design



(25-patient cohorts)

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Our vision for selective CDK7 inhibition in difficult-to-treat cancers

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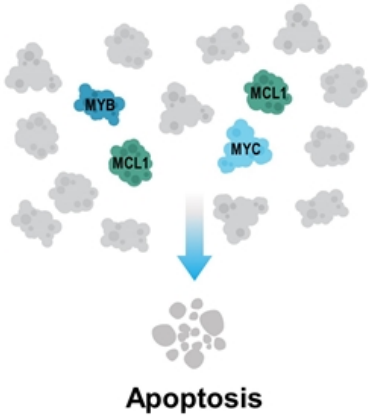
Selective CDK7 inhibition attacks two fundamental processes in cancer

Transcription

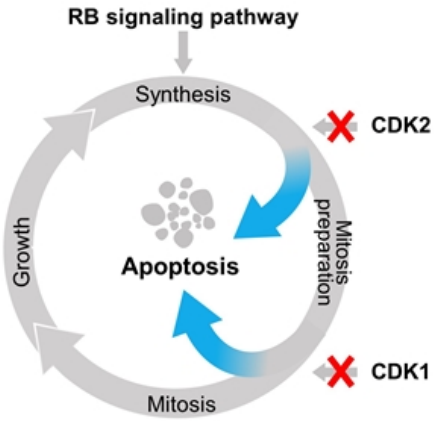
Selectively inhibiting CDK7 has been shown preclinically to decrease expression of oncogenic transcription factors and anti-apoptotic proteins



CDK7

Cell cycle

Selectively inhibiting CDK7 is thought to interfere with cancer-driving adaptations at multiple points in the cell cycle, promoting the induction of apoptosis



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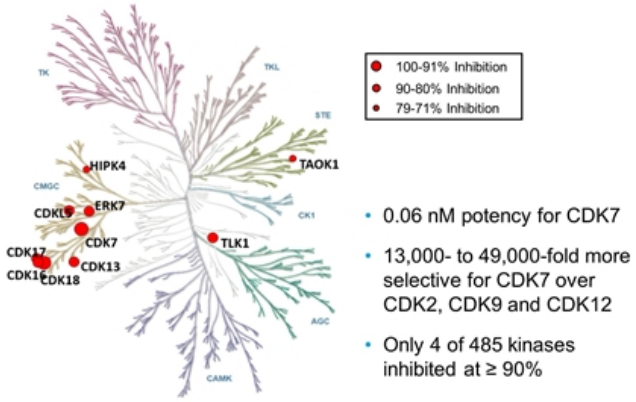
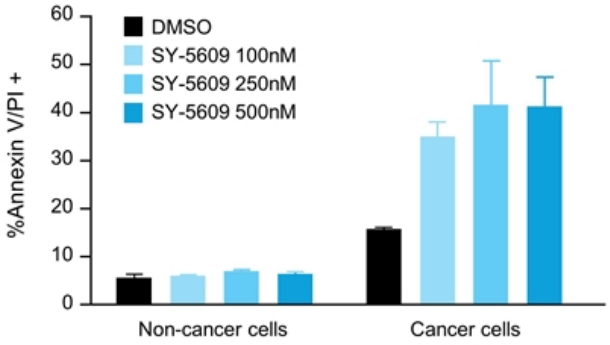
SY-5609: A highly selective oral CDK7 inhibitor with best-in-class potential



- 0.06 nM potency for CDK7
- 13,000- to 49,000-fold more selective for CDK7 over CDK2, CDK9 and CDK12
- Only 4 of 485 kinases inhibited at ≥ 90%

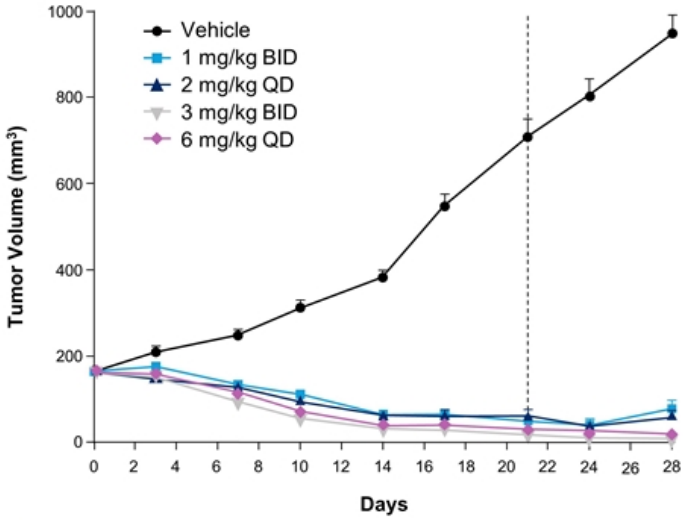
Induced apoptosis in cancer cells but not in non-cancer cells



Data presented in October 2019 at EORTC-NCI-AACR Conference

SY-5609 shows tumor growth inhibition, including regressions, below MTD in preclinical models

Triple negative breast cancer model



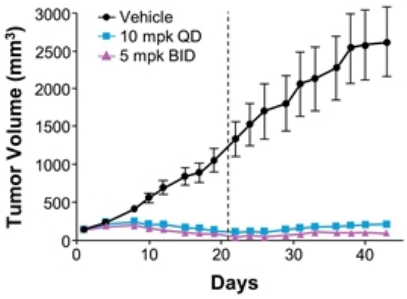
- Regressions observed at 5-fold below MTD of ≥10 mg/kg QD

----- Dashed lines represent end of treatment

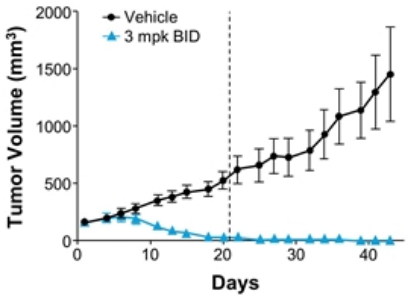
Data presented in October 2019 at EORTC-NCI-AACR Conference

SY-5609 shows robust anti-tumor activity, including complete regressions, in preclinical models of multiple solid tumors

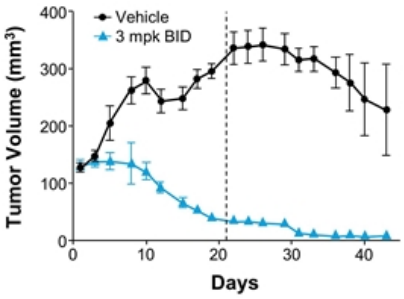
Triple-negative breast cancer model



Small-cell lung cancer model



High-grade serous ovarian cancer model



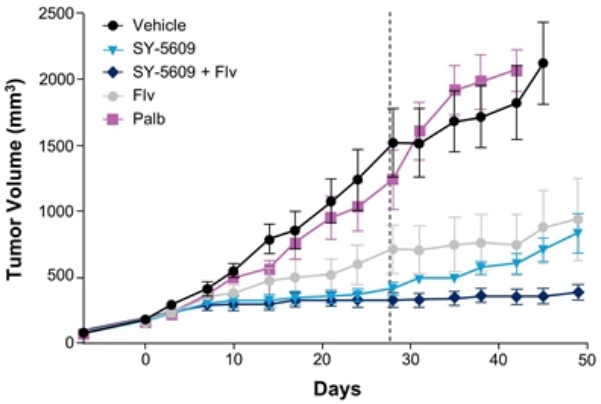
100% (12/12) models tested demonstrated substantial tumor growth inhibition

58% (7/12) demonstrated deep and sustained regressions

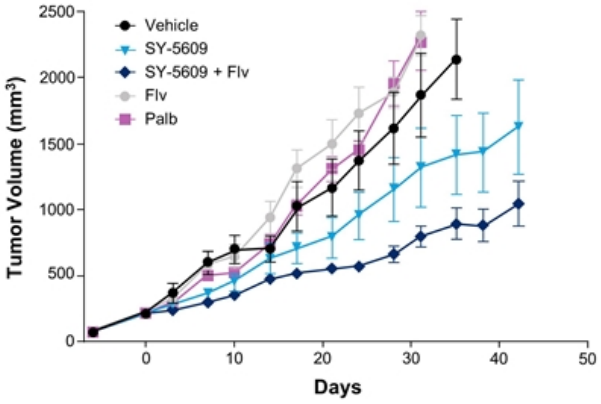
Dashed lines represent end of treatment

SY-5609 induces robust responses in preclinical treatment-resistant ER+ breast cancer models

CDK4/6 inhibitor resistant model



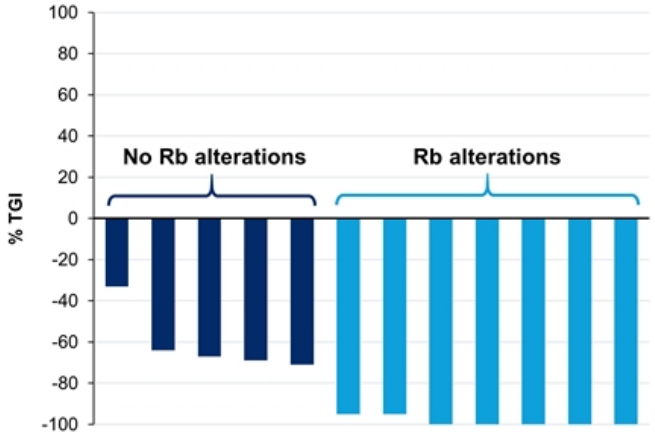
CDK4/6 inhibitor and hormonal resistant model



Palb: palbociclib, 50mg/kg once daily, oral; **Flv**: fulvestrant, 2.5mg/kg once weekly, sub-cutaneuous, **SY-5609**: 6 mg/kg once daily, oral

Deeper and more sustained responses associated with Rb alterations in preclinical studies of breast, lung and ovarian cancers

Tumor growth inhibition in all breast, lung and ovarian cancer PDX models tested



Supports planned Phase 1 trial enriched for populations with Rb alterations

- 29% of basal breast cancer patients[1]
- ~1/3 of HR+ breast cancer patients post CDK4/6 inhibitors[2]
- 75-90% of small cell lung cancer patients[3]
- 67% of high-grade serous ovarian cancer patients[4]

[1]TCGA Breast Cancer Integrated Analysis, Nature 2012
[2] Spring et al., San Antonio Breast Cancer Symposium 2018
[3]Cancer Med. 2019 Apr; 8(4): 1459–146
[4]TCGA Ovarian Cancer Integrated Analysis, Nature 2011

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Data presented in October 2019 at EORTC-NCI-AACR Conference

Expect to initiate Phase 1 trial in select solid tumors in Q1 2020

- On track to complete IND-enabling studies by year-end
- Dose escalation will enroll patients with select solid tumors
- Focusing on patient populations we believe are enriched for response, including:
  - Breast
  - Lung
  - Ovarian
  - Solid tumors of any histology harboring RB alterations

Robust early-stage pipeline to fuel long-term growth

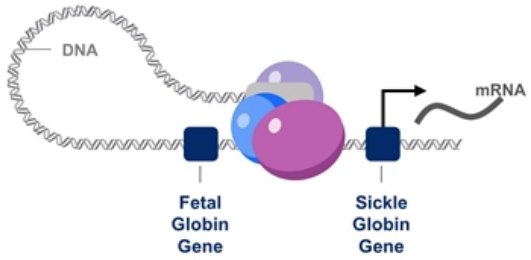
	Program	Target Development	Drug Discovery	IND-Enabling
Cancer	CDK12/13 inhibitor			
	Macrophage target			
	Cancer			
Monogenic Disease	Sickle cell disease			
	Other monogenic diseases			
Partnered (Incyte)	Myeloproliferative neoplasms			

Monogenic disease: Alter expression of a single gene for therapeutic benefit

Sickle cell disease (SCD)

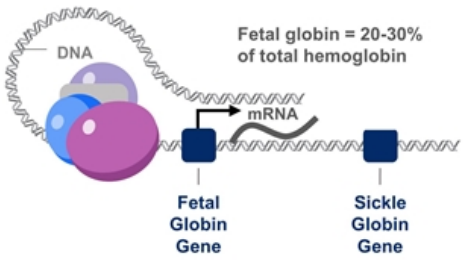
Clinical and genetic data point to therapeutic benefit of elevated fetal globin

- SCD caused by mutated adult globin gene
- Fetal globin gene typically turned off at birth
- In some SCD patients, the fetal globin gene remains on and is associated with milder disease



Using gene control platform to elevate fetal globin expression

- Characterized transcriptional programs that determine globin expression in fetal and adult states
- Identifying gene regulatory interactions at the globin locus
- Targeting transcriptional regulators with small molecules at the globin genes



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Milestones expected in 2019 and 2020

	Q4 2019	2020
SY-1425	✓ Updated data in ND unfit AML ✓ Completed enrollment in ND unfit AML	Potential POC in R/R AML
SY-5609	Complete IND-enabling studies	Initiate Phase 1 oncology trial in Q1 2020
Discovery	ASH oral presentation on sickle cell SABCS presentation on metastasis in TNBC	

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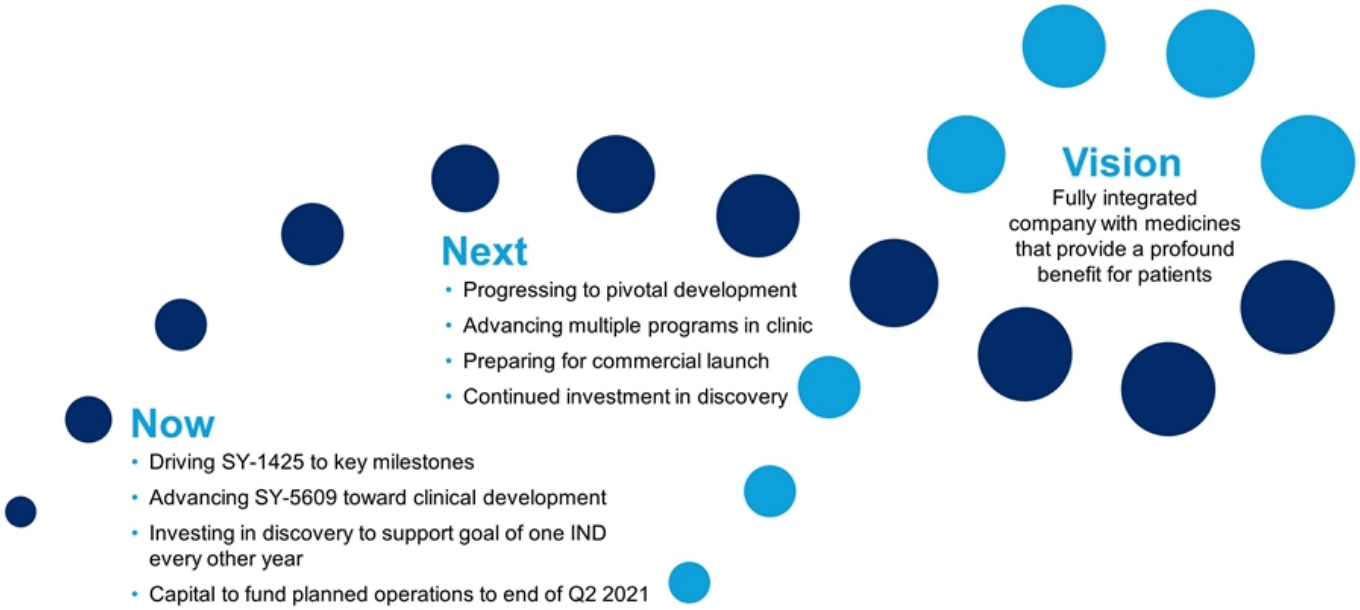
Rapidly advancing toward our vision



Vision

Fully integrated company with medicines that provide a profound benefit for patients

Next

- Progressing to pivotal development
- Advancing multiple programs in clinic
- Preparing for commercial launch
- Continued investment in discovery

Now

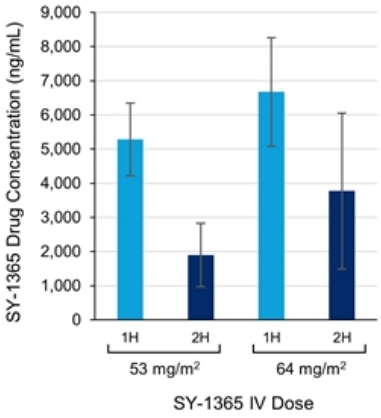
- Driving SY-1425 to key milestones
- Advancing SY-5609 toward clinical development
- Investing in discovery to support goal of one IND every other year
- Capital to fund planned operations to end of Q2 2021

SYROS

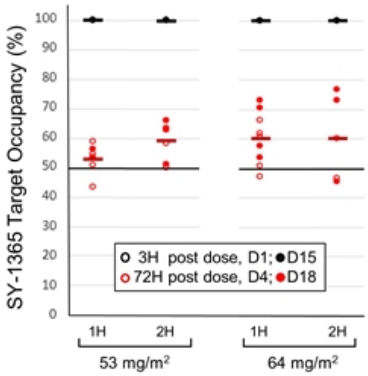

SYROS

Peri-infusional AEs in Phase 1 trial were associated with peak blood SY-1365 concentrations and not CDK7 target engagement

SY-1365 Plasma Cmax



SY-1365 Target Engagement



Infusion-associated Adverse Events (≥ 20%)*

Preferred Term	All Grades n (%)		≥ Grade 3 n (%)	
	N = 31	N = 24	N = 31	N = 24
	1 hour	2 hour	1 hour	2 hour
Headache	19 (61)	12 (50)	2 (6)	0 (0)
Nausea	12 (39)	5 (21)	1 (3)	0 (0)
Vomiting	10 (32)	1 (4)	1 (3)	0 (0)

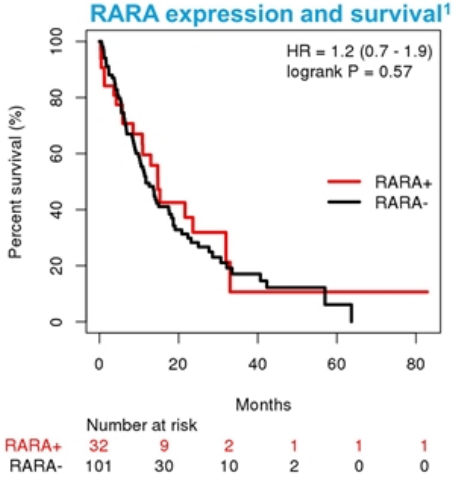
*Includes AEs experienced in patients treated with 53 mg/m² and 64 mg/m²

Longer infusions maintained CDK7 target engagement while lowering peak drug concentrations and decreasing frequency and severity of peri-infusional AEs

SYROS

RARA is not a prognostic biomarker in AML patients

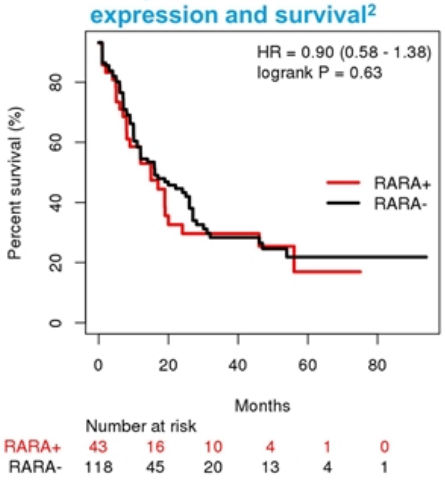
Analysis of BeatAML Registry RARA expression and survival[1]



Number at risk

RARA+	32	9	2	1	1	1
RARA-	101	30	10	2	0	0

Analysis of TCGA RARA expression and survival[2]



Number at risk

RARA+	43	16	10	4	1	0
RARA-	118	45	20	13	4	1

- Independent analyses of BeatAML[1], TCGA[2], and AML patient sample analyses[3] show that prognosis is similar regardless of levels of RARα expression

[1] Tyner et al., Functional Genomic Landscape of Acute Myeloid Leukaemia, Nature 2018
[2] TCGA Research Network, Genomic and Epigenomic Landscapes of Adult De Novo Acute Myeloid Leukemia, NEJM 2013; Expression and survival data from PanCancerAtlas portal on GDC: https://gdc.cancer.gov/about-data/publications/pancanatlas
[3] McKeown et al., Superenhancer Analysis Defines Novel Epigenomic Subtypes of Non-APL AML, Including an RARα Dependency Targetable by SY-1425, a Potent and Selective RARα Agonist, Cancer Discovery 2017

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