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): April 24, 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.)**

620 Memorial Drive, Suite 300 **Cambridge, Massachusetts**	**02139**
(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 (*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))

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

On April 24, 2019, we conducted an investor event focused on the unmet need, treatment landscape and opportunities for selective cyclin-dependent kinase 7 inhibition in ovarian and breast cancers. The slide presentation we made during this event 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 April 24, 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: April 24, 2019

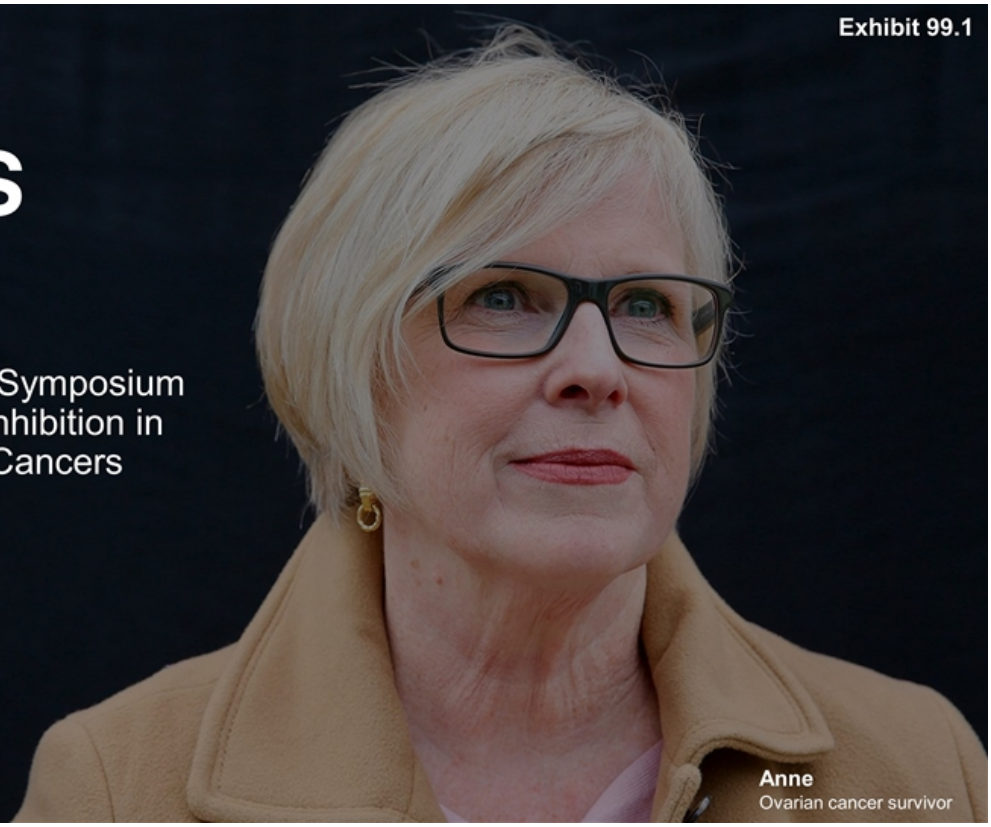
By: /s/ Gerald E. Quirk
Gerald E. Quirk
Chief Legal & Administrative Officer

Exhibit 99.1

SYROS

Key Opinion Leader Symposium on Selective CDK7 Inhibition in Ovarian and Breast Cancers

April 24, 2019

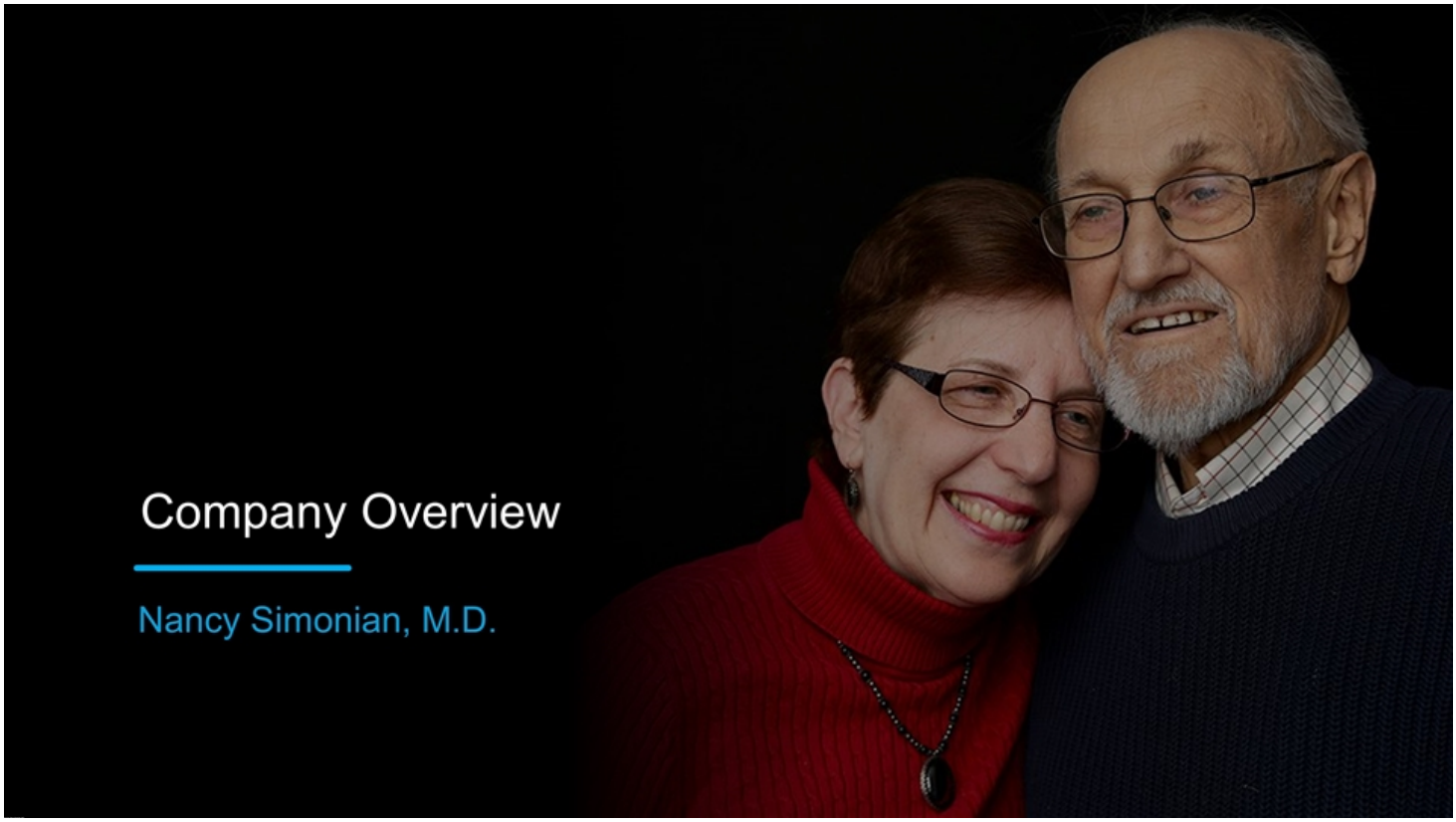


Forward-looking statements

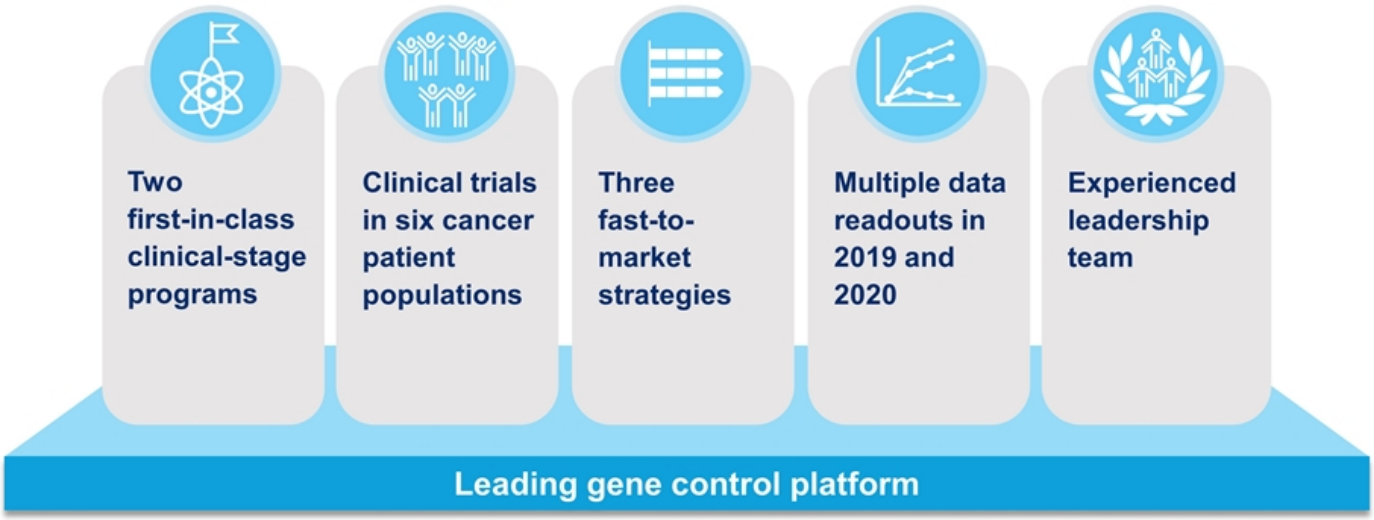
This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this presentation, including statements regarding 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-1365, under the timelines we project in current and future clinical trials or to achieve clinical proof of concept in these trials; 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 and toxicology studies; replicate scientific and non-clinical data in clinical trials; successfully develop a companion diagnostic test to identify patients with the *RARA* and *IRF8* biomarkers; 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 that 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.

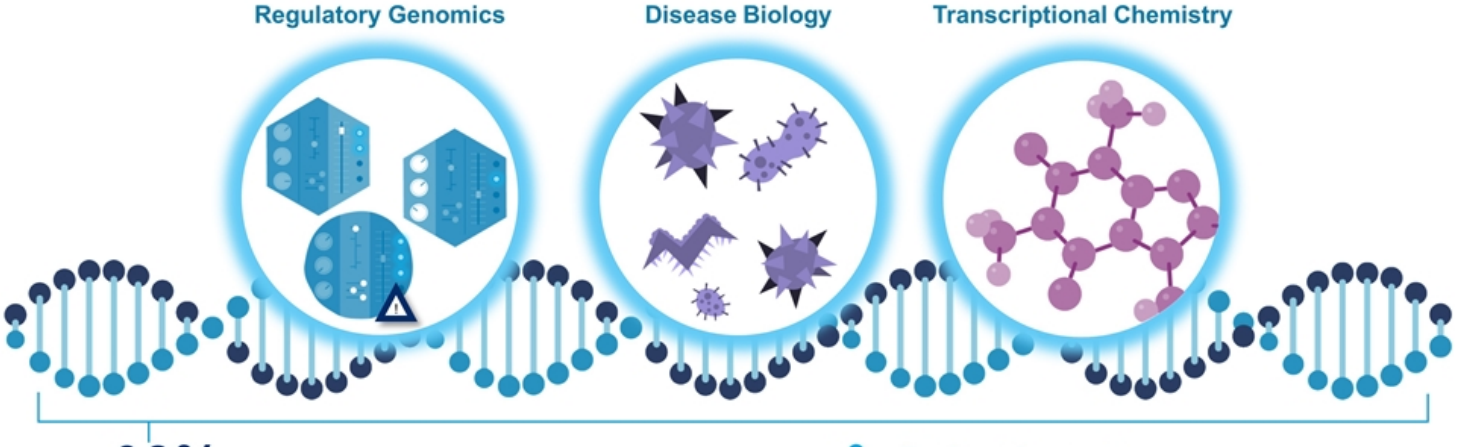

Company Overview
Nancy Simonian, M.D.

Syros today: Clear vision, growing pipeline, pioneering platform



Pioneering a new approach: Medicines that control the expression of genes

Our leading gene control platform

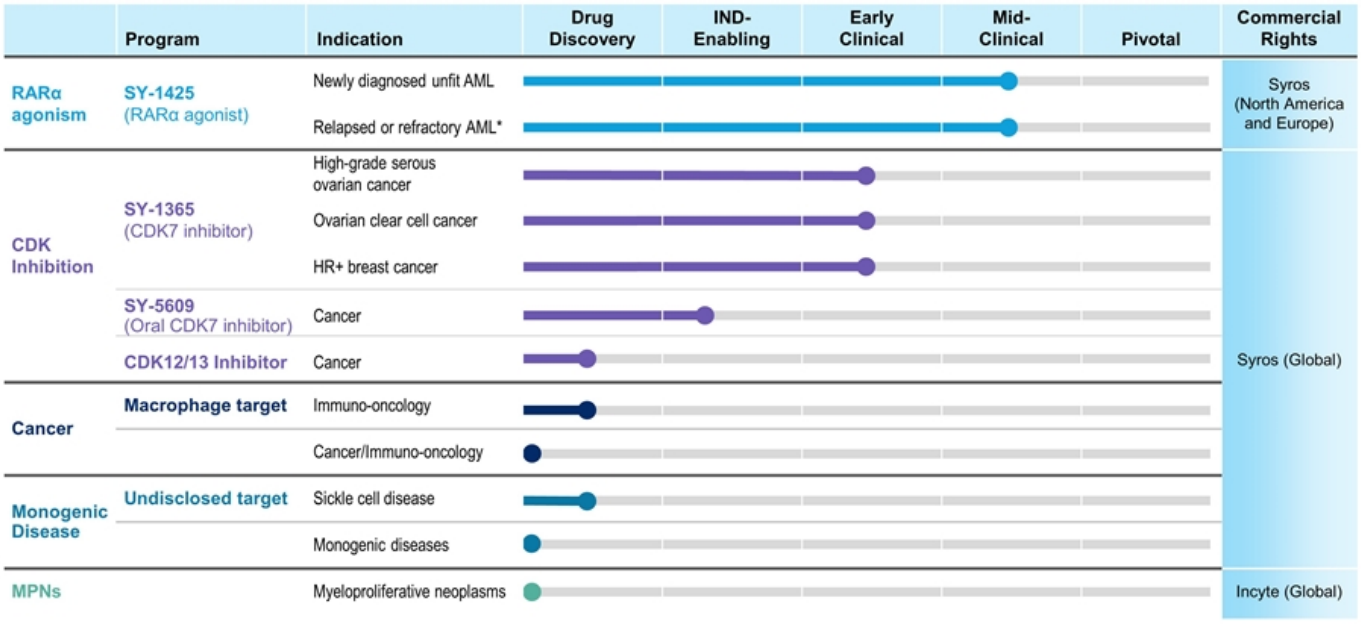


98% Previously unexplored regulatory regions of the genome control the expression of genes determining cell function; majority of disease variation found in these regions

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

SYROS

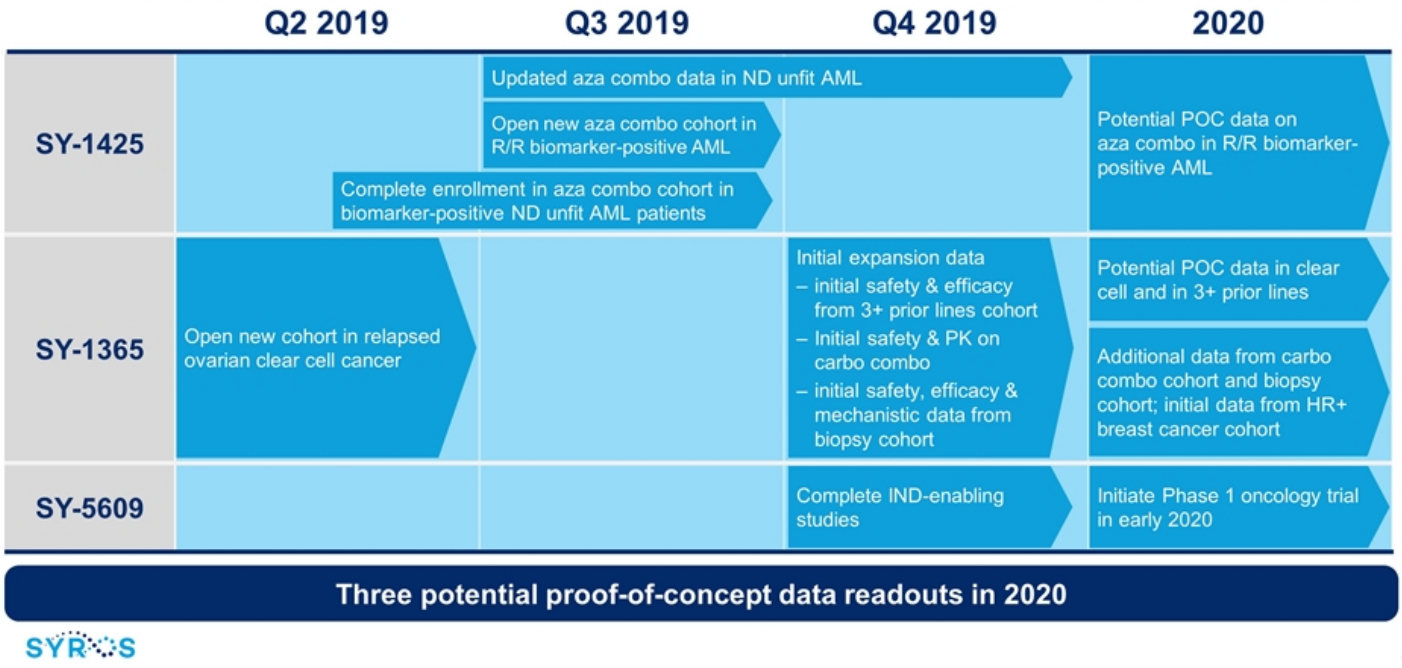
Deep and growing pipeline with multiple potential first-in-class programs



SY-1425 is approved in Japan as Amnolake® (tamibarotene) for patients with relapsed/refractory APL
* Expected to begin in Q3 2019

Realizing our vision for the promise of selective CDK7 inhibition in difficult-to-treat cancers

Multiple clinical milestones expected in 2019 and 2020



Three potential proof-of-concept data readouts in 2020

SYROS

Overview of Syros' CDK7 Franchise

David Roth, M.D.

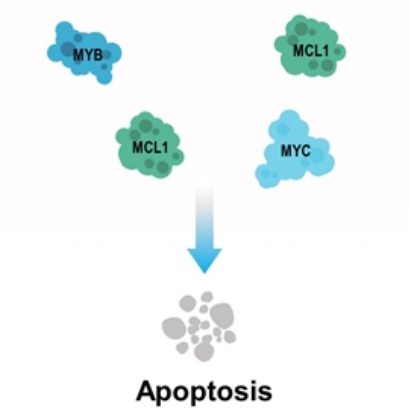
Selective CDK7 inhibition attacks two fundamental processes in cancer

Transcription

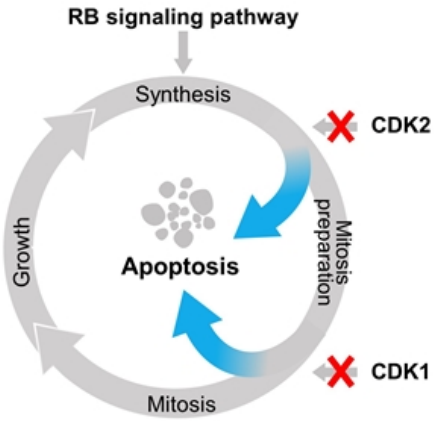
CDK7

Cell cycle

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



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



SYROS

Exploring SY-1365 as single agent and in combination in ovarian and breast cancer patients, including two potential fast-to-market strategies

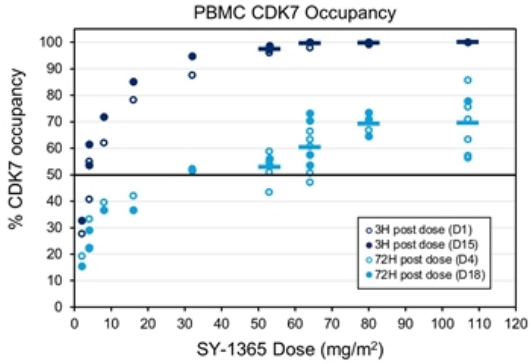
- Initial data from relapsed HGSOC and biopsy cohorts expected in Q4 2019, with additional data expected in 2020
- Potential proof-of-concept data in clear cell and relapsed HGSOC (3+ prior lines) expected in 2020
- Initial data from HR-positive breast cancer cohort expected in 2020

Ongoing expansion cohorts		
Patient population	**Single/combo agent**	**Target enrollment**
Relapsed ovarian clear cell cancer	Single agent	N=12
Relapsed HGSOC, 3+ prior lines	Single agent	N=24
Relapsed HGSOC, 1+ prior lines (platinum sensitive)	Combination with carboplatin	N=24
HR+ metastatic breast cancer, CDK4/6 inhibitor resistant	Combination with fulvestrant	N=12
Solid tumors accessible for biopsy	Single agent	N=30

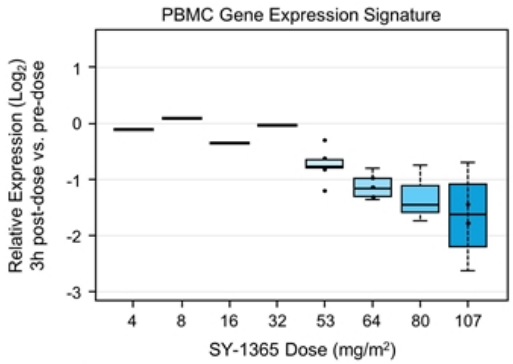
SYROS

SY-1365 demonstrated proof-of-mechanism at tolerable doses in dose escalation portion of ongoing Phase 1 trial

Exceeded desired target occupancy levels at doses ≥ 32 mg/m²



Demonstrated dose-dependent downstream changes in gene expression



Adverse events (AEs) were predominantly low grade, reversible and generally manageable

- Most frequent related AEs include headache, nausea, vomiting and fatigue
- No reports of neutropenia

Data as of October 15, 2018; Presented in November 2018 at EORTC-NCI-AACR Symposium

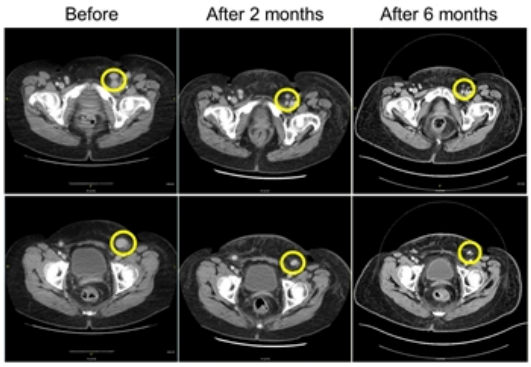
SY-1365 demonstrated early evidence of clinical activity, including durable partial response in relapsed ovarian clear cell cancer patient

SY-1365 demonstrated 37% disease control rate (CR+PR+SD)

- Clinical activity per RECIST 1.1 criteria observed in 7 of 19 evaluable patients*
  - 1 confirmed PR (clear cell ovarian cancer patient) observed at 80 mg/m^2 BIW
  - 6 stable disease (2 ovarian, 2 breast and 2 endometrial cancer patients), mostly at doses ≥ 32 mg/m^2 BIW
- Duration of treatment ranged from 50 - 127 days

* Response evaluable patients include 5 ovarian, including 1 clear cell ovarian, 5 breast and 3 endometrial cancer patients

CT images of heavily pretreated stage IV clear cell ovarian cancer patient



- Confirmed PR after 2 cycles (31.8% reduction at C3D1)
- Remained on study in PR in 7th month of SY-1365 treatment as of data snapshot (49% decrease at C7D1)
- Best response to prior therapies was stable disease

Data as of October 15, 2018; Presented in November 2018 at EORTC-NCI-AACR Symposium

RB pathway alterations predict response to SY-1365 in ovarian cancer PDX models, pointing to potential biomarker-driven patient enrichment strategy

90% of models with RB alterations responded to SY-1365

Ovarian Subtype	Response Class	% TGI
Clear Cell	Responder	86
Serous	Responder	84
Serous	Responder	81
Serous	Responder	75
Serous	Responder	74
Serous	Responder	74
Serous	Responder	62
Serous	Responder	55
Serous	Responder	51
Serous	Non Responder	34

RB pathway alterations prospectively defined per TCGA criteria – including RB1 deletion or mutation, CDKN2A downregulation or deletion, CCNE1 amplification, CCND1 amplification, or CCND2 upregulation

Supports ongoing development in ovarian and CDK4/6 inhibitor-resistant breast cancer patients

- Approximately 2/3 of high-grade serous ovarian cancer patients have RB alterations[1]
- Approximately half of ovarian clear cell cancer patients have deleted or amplified genes in RB or cell cycle pathways[2]
- Approximately 1/3 of HR+ breast cancer patients acquire RB or cell cycle alterations post CDK4/6 inhibitors[3]

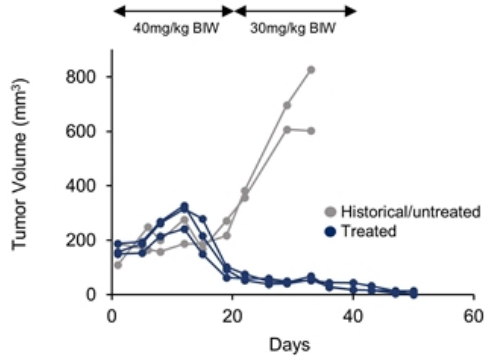
[1] TCGA Ovarian Cancer Integrated Analysis, Nature 2011
[2] Murakami et al., Am J Pathol. 2017 Oct;187(10):2246-2258
[3] Spring et al., San Antonio Breast Cancer Symposium 2018

SYROS

Data presented in April 2019 at AACR Annual Meeting

SY-1365 shows anti-tumor activity as single agent and in combination with standard-of-care in ovarian models, supporting ongoing clinical investigation

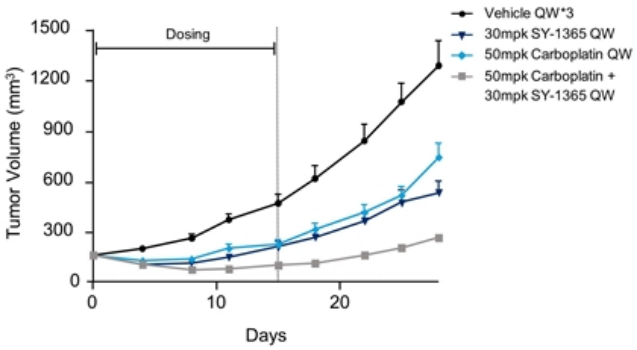
SY-1365 induces tumor growth inhibition, including complete regressions, in heavily pretreated ovarian cancer models



- Responses observed in 10/17 (59%) models, irrespective of BRCA status or PARP inhibitor sensitivity

Data presented in April 2018 at the American Association of Cancer Research (AACR) Annual Meeting

Weekly SY-1365 in combination with carboplatin enhances activity in ovarian cancer xenograft models



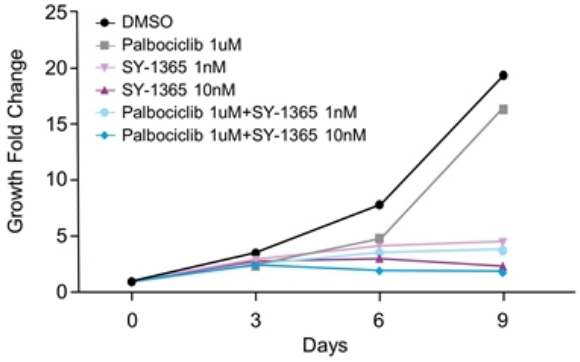
- SY-1365 inhibited DNA repair and transcription of HRR genes in preclinical models, inducing an HRD-like state that may increase sensitivity to DNA-damaging agents and DNA repair inhibitors

Data presented in November 2018 at EORTC-NCI-AACR Symposium

SYROS

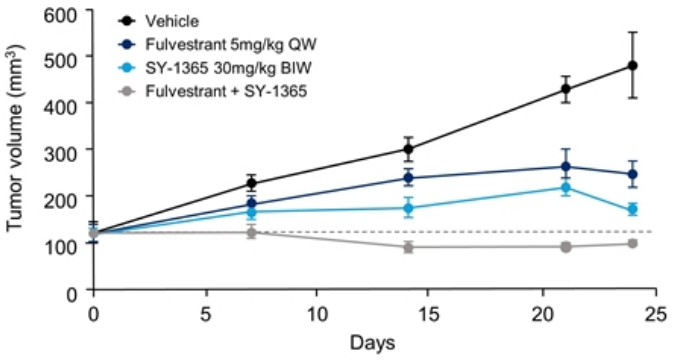
SY-1365 shows anti-tumor activity and synergy with fulvestrant in HR-positive breast cancer models, including CDK4/6 inhibitor resistant models

SY-1365 inhibits growth of CDK4/6 inhibitor resistant breast cancer cell models



Data presented by Syros' collaborators at Dana-Farber Cancer Institute in December 2018 at San Antonio Breast Cancer Symposium

HR-positive CDX model



In vitro synergy was seen in several HR+ breast cancer cell lines

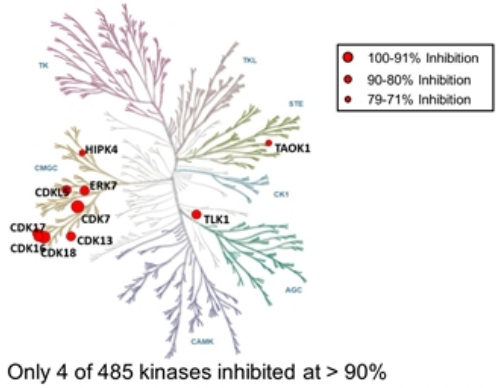
Source: Jeselsohn et al, 2018; Data from collaboration with Dana-Farber Cancer Institute

SYROS

SY-5609: A potent and highly selective oral CDK7 inhibitor

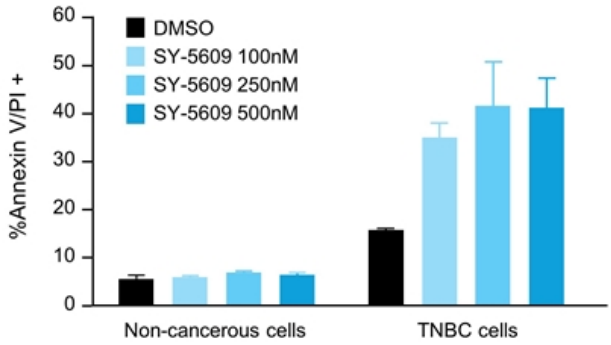
- Significant opportunity for adding an oral approach across a range of solid tumors and blood cancers
- Expect to initiate a Phase 1 oncology trial for SY-5609 in early 2020

SY-5609 is a potent and highly selective oral CDK7 inhibitor



- Only 4 of 485 kinases inhibited at > 90%
- 13,000- to 49,000-fold greater selectivity for CDK7 over other CDK family members

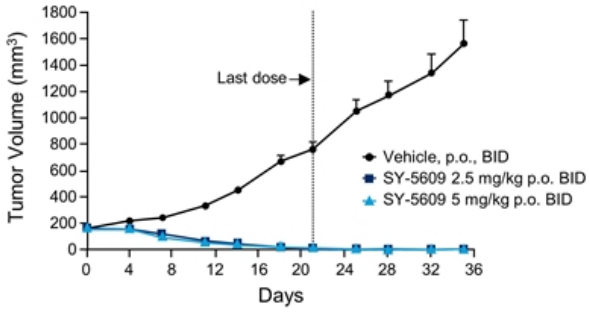
SY-5609 induced apoptosis in cancer cells but not in non-cancerous cells



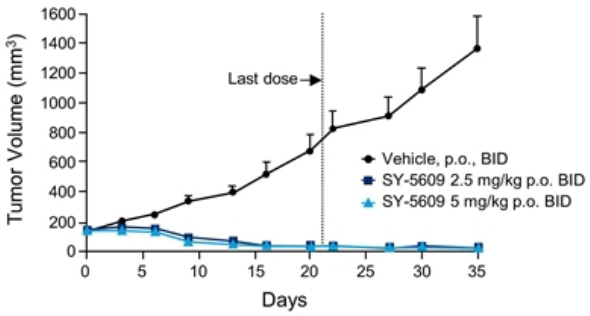
Data presented in April 2019 at AACR Annual Meeting

SY-5609 demonstrates substantial tumor growth inhibition as a single agent in multiple breast and ovarian cancer models

Triple Negative Breast Cancer CDX Model



Ovarian Cancer CDX Model



- Complete regressions observed in multiple TNBC and ovarian CDX models at doses below the MTD
- Modulation of downstream markers, including MCL1, observed in tumor tissues, confirming CDK7 inhibition *in vivo*
- Substantial tumor growth inhibition also observed in multiple PDX models with doses below MTD

SYROS

Data presented in April 2019 at AACR Annual Meeting

Key takeaways

- Selective CDK7 inhibition represents a potentially transformative targeted approach for many difficult-to-treat cancers
- SY-1365 is a first-in-class selective CDK7 inhibitor in Phase 1 trial
- Initial development is focused on ovarian and breast cancers based on mechanistic rationale, preclinical data and unmet need and supported by early clinical signals
- Unmet need in relapsed ovarian and metastatic HR-positive breast cancers is significant
- Ongoing Phase 1 trial supports potential fast-to-market strategies and opportunities to move into earlier lines of treatment and emerging patient populations
- Syros is building on its CDK7 leadership with SY-5609, a highly selective oral CDK7 inhibitor, that together with SY-1365 could make for a powerful CDK7 franchise


SYROS