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): **March 12, 2018**

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** (Address of Principal Executive Offices)	**02139** (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 2.02. Results of Operations and Financial Condition

On March 12, 2018, we announced our financial results for the quarter and year ended December 31, 2017. The full text of the press release issued in connection with the announcement is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

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 March 2018, is furnished as Exhibit 99.2 to this Current Report on Form 8-K.

* * *

The information responsive to Items 2.02 and 7.01 of this Form 8-K and Exhibits 99.1 and 99.2 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	Press release dated March 12, 2018
99.2	Slide presentation dated March 2018

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: March 15, 2018

By: /s/ Joseph J. Ferra, Jr.
Joseph J. Ferra, Jr.
Chief Financial Officer

Exhibit 99.1

Syros Reports Fourth Quarter and Full Year 2017 Financial Results and Highlights Recent Accomplishments and Anticipated Milestones

Announced Global Collaboration with Incyte to Use Propriety Gene Control Platform to Identify Novel Therapeutic Targets in Myeloproliferative Neoplasms

Announced Closing of $46 Million Public Offering of Common Stock, Including Full Exercise of Underwriters' Option to Purchase Additional Shares

Presented Initial Clinical Data from Ongoing Phase 2 Trial of SY-1425 Showing Biological and Clinical Activity as Single Agent in Genomically Defined AML and MDS Patients and Supporting Combination Strategy

Initial Data from Combination Arms of Phase 2 Trial of SY-1425 and Dose Escalation Portion of Phase 1 Trial of SY-1365 Expected in Fourth Quarter of 2018

CAMBRIDGE, Mass., March 12, 2018 — Syros Pharmaceuticals (NASDAQ: SYRS), a biopharmaceutical company pioneering the discovery and development of medicines to control the expression of genes, today reported financial results for the fourth quarter and year ended December 31, 2017 and provided an update on recent accomplishments and planned upcoming events.

"2017 was an important year for Syros, marked by clinical and preclinical data for SY-1425 and SY-1365 that lay a clear path forward for the further development of both programs," said Nancy Simonian, M.D., Chief Executive Officer of Syros. "Additionally, our pioneering gene control platform continued to deliver, enabling us to expand our early-stage pipeline in cancer and monogenic diseases and enter into a collaboration with Incyte designed to allow us to benefit patients with diseases beyond our current areas of focus. We built on our strong foundation, adding to the leadership team and fortifying our cash position to fund our planned operations into 2020 and drive SY-1425 and SY-1365 to key value inflection points. As we enter 2018, we believe we are well-positioned to execute on our near-term and long-term goals to achieve our vision of becoming a fully integrated biopharmaceutical company with medicines that provide a profound and durable benefit for patients."

Upcoming Milestones

- Syros plans to report clinical data in the fourth quarter of 2018 from a cohort in its ongoing Phase 2 trial evaluating SY-1425 in combination with azacitidine in *RARA* and *IRF8* biomarker-positive newly diagnosed acute myeloid leukemia (AML) patients who are not suitable candidates for standard chemotherapy.
- Syros plans to report clinical data in the fourth quarter of 2018 from a pilot cohort in its ongoing Phase 2 trial evaluating SY-1425 in combination with daratumumab in *RARA* and *IRF8* biomarker-positive relapsed or refractory AML and higher-risk myelodysplastic syndrome (MDS) patients.
- Syros plans to open expansion cohorts in mid-2018 in its ongoing Phase 1 trial of SY-1365 evaluating it as a single agent and in combination with carboplatin in multiple ovarian cancer patient populations. Based on emerging preclinical data showing anti-tumor activity of SY-1365 in hormone receptor-positive (HR-positive) breast cancer

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models, the Company announced today that it also plans to add an expansion cohort evaluating SY-1365 in combination with fulvestrant in HR-positive metastatic breast cancer patients who progress after treatment with a CDK4/6 inhibitor plus an aromatase inhibitor.
- Syros plans to report clinical data in the fourth quarter of 2018 from the dose escalation portion of its ongoing Phase 1 trial of SY-1365 in advanced solid tumor patients.
- Syros plans to select a new development candidate from its preclinical pipeline by the end of 2018.

Recent Platform and Pipeline Highlights

- In January 2018, Syros announced that the U.S. Patent and Trademark Office issued two patents covering methods for stratifying patients with AML and MDS for treatment with SY-1425.
- In January 2018, Syros announced a clinical supply agreement with Janssen Research and Development. Under the terms of the agreement, Janssen is supplying daratumumab for the combination dosing cohort in biomarker-positive relapsed or refractory AML and higher-risk MDS patients in Syros' ongoing Phase 2 trial of SY-1425.
- In December 2017, Syros presented initial clinical data from its ongoing Phase 2 trial of SY-1425 in biomarker-positive patients with AML and MDS at the American Society of Hematology (ASH) Annual Meeting, showing biological and clinical activity as a single agent and supporting ongoing development of SY-1425 in combination with other therapies:
    - Clinical activity was observed in 43% of evaluable relapsed or refractory AML and higher-risk MDS patients, including improvement in blood counts and reductions in bone marrow blasts.
    - Myeloid differentiation was observed, including the induction of CD38 in 85% of evaluable patients.
    - SY-1425 generally well-tolerated with chronic, daily dosing with the majority of adverse events being low grade.

- In December 2017, Syros presented new preclinical data on SY-1365 at ASH. The data showed anti-tumor activity in leukemia and lymphoma cell lines and *in vivo* models of AML. Additionally, the data pointed to a potential biomarker of response to SY-1365 and demonstrated synergistic activity with venetoclax, a BCL2 inhibitor, in preclinical AML models.
- In December 2017, Syros presented new preclinical data on SY-1365 at the San Antonio Breast Cancer Symposium (SABCS). The data demonstrated anti-tumor activity across a broad panel of breast cancer cell lines and pointed to potential biomarkers of response. Syros also presented on its analysis of regulatory regions of the genome in cancer stem cell-enriched triple negative breast cancer (TNBC) cell lines, which revealed key genes that may be involved in driving disease relapse and metastasis in TNBC and suggest potential new targets for future drug discovery and development.

Recent Corporate Highlights

- Syros today announced the appointment of Joseph J. Ferra as Chief Financial Officer.
- In January 2018, Syros announced the closing of an underwritten public offering of 4,816,753 shares of common stock at a public offering price of $9.55 per share, including the exercise in full by the underwriters of their option to purchase additional shares of common stock. Syros received aggregate gross proceeds of

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approximately $46 million, before deducting underwriting discounts and commissions and estimated offering expenses. In connection with the offering, Incyte Corporation, exercised its right to purchase shares of Syros common stock directly from the company at the public offering price, in a concurrent private placement, resulting in proceeds of approximately $1.4 million.
- In January 2018, Syros announced a global target discovery and validation collaboration with Incyte focused on myeloproliferative neoplasms (MPNs). Under the terms of the agreement, Syros will use its proprietary platform to identify novel therapeutic targets with a focus in MPNs. Incyte has options to obtain exclusive worldwide rights to intellectual property resulting from the collaboration for up to seven validated targets and, upon exercise of its options, will have exclusive worldwide rights to develop and commercialize any therapies under the collaboration that modulate those validated targets. Incyte paid Syros $10 million in upfront cash and purchased a total of $10 million in Syros common stock at a price of $12.61 per share. In addition, Syros could receive up to $54 million from Incyte in target validation and option exercise fees and up to $115 million in potential development, regulatory and commercial milestone payments per target for up to seven validated targets, plus low single-digit royalties on sales of products that result from the collaboration.
- In November 2017, Syros announced the appointment of Jeremy P. Springhorn, Ph.D., as Chief Business Officer.

Fourth Quarter 2017 Financial Results

Cash, cash equivalents and marketable securities as of December 31, 2017 were $72.0 million, compared with $83.6 million on December 31, 2016. Cash, cash equivalents and short-term investments as of December 31, 2017 do not include the aggregate gross proceeds of approximately $46 million from Syros' underwritten public offering of common stock, which closed in February 2018, the $1.4 million in proceeds from the private placement of stock with Incyte concurrent with the public offering, or the $10 million upfront payment and purchase of $10 million in Syros common stock received in January 2018 in connection with entry into the collaboration with Incyte.

For the fourth quarter of 2017, Syros reported a net loss of $15.3 million, or $0.58 per share, compared to a net loss of $11.0 million, or $0.47 per share, for the same period in 2016. Stock-based compensation included in the net loss was $1.3 million for the fourth quarter of 2017, compared to $0.7 million for the same period in 2016.

- Research and development (R&D) expenses were $11.8 million for the fourth quarter of 2017, as compared to $8.4 million for the same period in 2016. Stock-based compensation included in R&D expenses was $0.5 million for the fourth quarter of 2017, compared to $0.2 million for the same period in 2016.
- General and administrative (G&A) expenses were $3.7 million for the fourth quarter of 2017, as compared to $2.9 million for the same period in 2016. Stock-based compensation included in G&A expenses was $0.8 million for the fourth quarter of 2017, compared to $0.5 million for the same period in 2016.

Full Year 2017 Financial Results

For the full year ended December 31, 2017, net loss was $54.0 million, or $2.13 per share, as compared to a net loss of $47.7 million, or $4.05 per share, for the same period in 2016.

Stock based compensation included in the net loss was $4.4 million for the year ended December 31, 2017, compared to $4.2 million for the same period in 2016.

- R&D expenses were $41.9 million for the year ended December 31, 2017, as compared to $37.8 million for the same period in 2016. The increase was due to an increase in expenses from third parties that conduct research and development and preclinical activities on our behalf, including an increase in clinical development costs for SY-1425 and SY-1365, offset by a decrease in preclinical development work for SY-1365 as toxicology studies were completed and the Phase 1 clinical trial was initiated. Stock-based compensation included in R&D expenses was $1.7 million for the year ended December 31, 2017, compared to $3.0 million for the same period in 2016.
- G&A expenses were $13.9 million for the year ended December 31, 2017, as compared to $10.5 million for the same period in 2016. The increase was largely due to an increase in employee-related costs, including salary, benefits and stock-based

compensation, as well as increased consulting, licensing, and professional fees to support the overall growth of the Company. Stock-based compensation included in G&A expenses was $2.7 million for the year ended December 31, 2017, compared to $1.2 million for the same period in 2016.

Financial Guidance

Based on its current plans, Syros believes that its cash, cash equivalents and short-term investments as of December 31, 2017, together with cash received in connection with entry into the collaboration with Incyte and the underwritten public offering and concurrent private placement of common stock that closed in February 2018, will be sufficient to enable it to fund its planned operating expense and capital expenditure requirements into 2020.

About Syros Pharmaceuticals

Syros is pioneering the understanding of the non-coding region of the genome to advance a new wave of medicines that control expression of genes. Syros has built a proprietary platform that is designed to systematically and efficiently analyze this unexploited region of DNA in human disease tissue to identify and drug novel targets linked to genomically defined patient populations. Because gene expression is fundamental to the function of all cells, Syros' gene control platform has broad potential to create medicines that achieve profound and durable benefit across a range of diseases. Syros is currently focused on cancer and monogenic diseases and is advancing a growing pipeline of gene control medicines. Syros' lead drug candidates are SY-1425, a selective RARα agonist in a Phase 2 clinical trial for genomically defined subsets of patients with acute myeloid leukemia and myelodysplastic syndrome, and SY-1365, a selective CDK7 inhibitor in a Phase 1 clinical trial for patients with advanced solid tumors. Led by a team with deep experience in drug discovery, development and commercialization, Syros is located in Cambridge, Mass.

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 the Company's ability to achieve its near- and long-term goals; its ability to advance its clinical-stage programs, including the reporting of clinical data from the combination cohorts of the ongoing Phase 2 clinical trial of SY-1425 and the dose escalation phase of the

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SY-1365 clinical trial in the fourth quarter of 2018, and the initiation of expansion cohorts of SY-1365 in ovarian and breast cancer in mid-2018; the selection of a development candidate for IND-enabling studies during 2018; the Company's ability to expand its early pipeline in cancer and monogenic diseases; the benefits of the Company's target discovery collaboration with Incyte; the Company's ability to fund its planned operations into 2020; and the benefits of Syros' gene control platform. The words ''anticipate,'' ''believe,'' ''continue,'' ''could,'' ''estimate,'' ''expect,'' ''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, including SY-1425 and SY-1365, 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; 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 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, including its ability to perform under the collaboration agreement with Incyte; 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, 2017, 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. Any forward-looking statements contained in this press release speak only as of the date hereof, and Syros expressly disclaims any obligation to update any forward-looking statements, whether because of new information, future events or otherwise.

Syros Pharmaceuticals, Inc.
Selected Condensed Consolidated Balance Sheet Data
(in thousands)
(unaudited)

	December 31, 2017	December 31, 2016
Cash, cash equivalents and marketable securities	$ 72,049	$ 83,593
Working capital(1)	60,746	75,941
Total assets	78,488	91,323
Total stockholders' equity	65,324	80,602

Syros Pharmaceuticals, Inc.
Condensed consolidated statements of operations
(in thousands, except share and per share data)
(unaudited)

	Three Months Ended December 31,		Years Ended December 31,	
	2017	2016	2017	2016
Revenue	$ —	$ 317	$ 1,101	$ 317
Operating expenses:				
Research and development	11,780	8,443	41,896	37,817
General and administrative	3,740	2,919	13,891	10,463
Total operating expenses	15,520	11,362	55,787	48,280
Loss from operations	(15,520)	(11,045)	(54,686)	(47,963)
Other income, net	218	80	676	220
Net loss	$ (15,302)	$ (10,965)	$ (54,010)	$ (47,743)
Accrued dividends on preferred stock	—	—	—	(3,681)
Net loss applicable to common stockholders	$ (15,302)	$ (10,965)	$ (54,010)	$ (51,424)
Net loss per share applicable to common stockholders - basic and diluted	$ (0.58)	$ (0.47)	$ (2.13)	$ (4.05)
Weighted-average number of common shares used in net loss per share applicable to common stockholders - basic and diluted	26,316,550	23,374,734	25,406,845	12,696,414

(1) The Company defines working capital as current assets less current liabilities. See the Company's consolidated financial statements for further details regarding its current assets and current liabilities.

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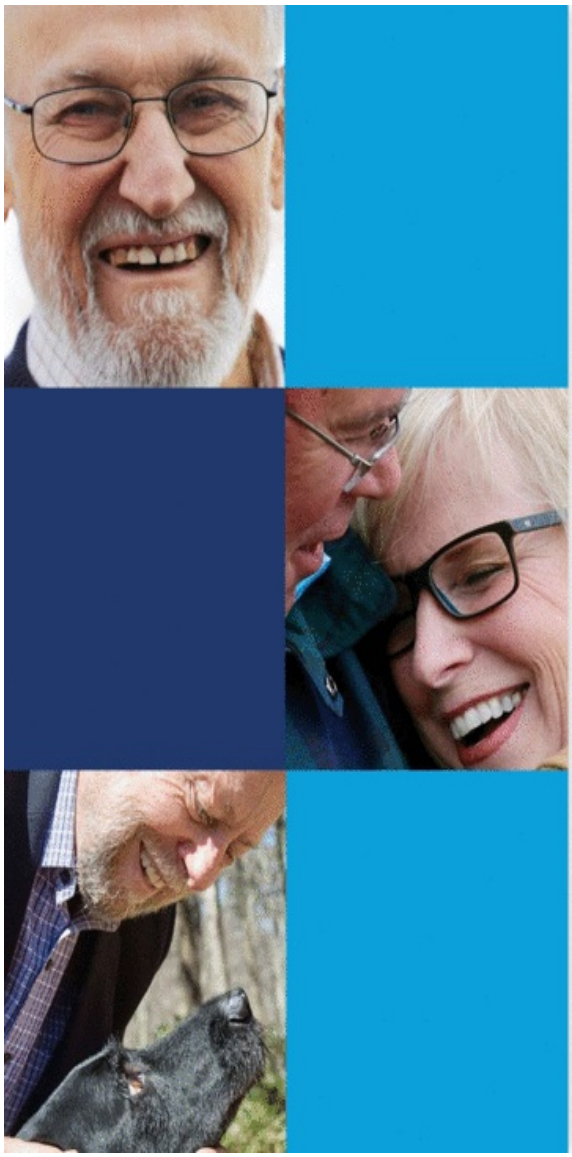
Exhibit 99.2



SYROS

An Expression Makes
a World of Difference

Company Overview

March 2018

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, and Syros' ability to: advance the development of its programs, including SY-1425 and SY-1365, under the timelines it projects in current and future clinical trials; advance discovery programs to identify drug candidates for IND-enabling studies; obtain and maintain patent protection for its drug candidates and the freedom to operate under third party intellectual property; demonstrate in any current and future clinical trials the requisite safety, efficacy and combinability of its drug candidates; replicate scientific and non-clinical data in clinical trials; successfully develop a companion diagnostic test to identify patients with *RARA* and *IRF8* biomarkers; 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, 2017, 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

Syros

Pioneering	First platform dedicated to the regulatory genome
Rapid translation	2 clinical-stage programs and 5 preclinical and discovery programs in less than 5 years
Productive	Product engine to advance goal of 1 IND every other year
Broad impact	Platform applicable across a wide array of diseases with focus on cancer, I/O and monogenic diseases
Strong foundation	Broad strategic optionality driven by experienced leadership team

Advancing our vision of transforming patients' lives

Advance first-in-class clinical programs	Leverage platform to fuel pipeline	Build on fundamentals for evolution toward fully integrated company

2018 objectives and milestones

SY-1425

- Report clinical data on SY-1425 combinations in Q4 2018

SY-1365

- Open Phase 1 expansions in ovarian and breast cancers in mid-2018
- Report clinical data from dose escalation in Q4 2018

- Select new development candidate
- Advance discovery programs in cancer/IO and sickle cell disease
- Execute on target discovery work in MPNs in collaboration with Incyte

- Continue to build development organization and capabilities
- Maintain financial discipline to execute on top priorities

Our platform integrates three areas of expertise

Regulatory genomics

- Whole genome analysis to identify dysregulated genes in patient subsets
- Single gene analysis to identify genomic regulatory elements controlling expression of genes
- Gene control biomarkers for patient selection and clinical acceleration

Transcriptional small molecule chemistry

- Biochemical, structural biology and medicinal chemistry expertise in targeting transcription
- Proprietary gene control compound library

Disease biology

Cancer

- Modulate transcription regulators to drive apoptosis or differentiation

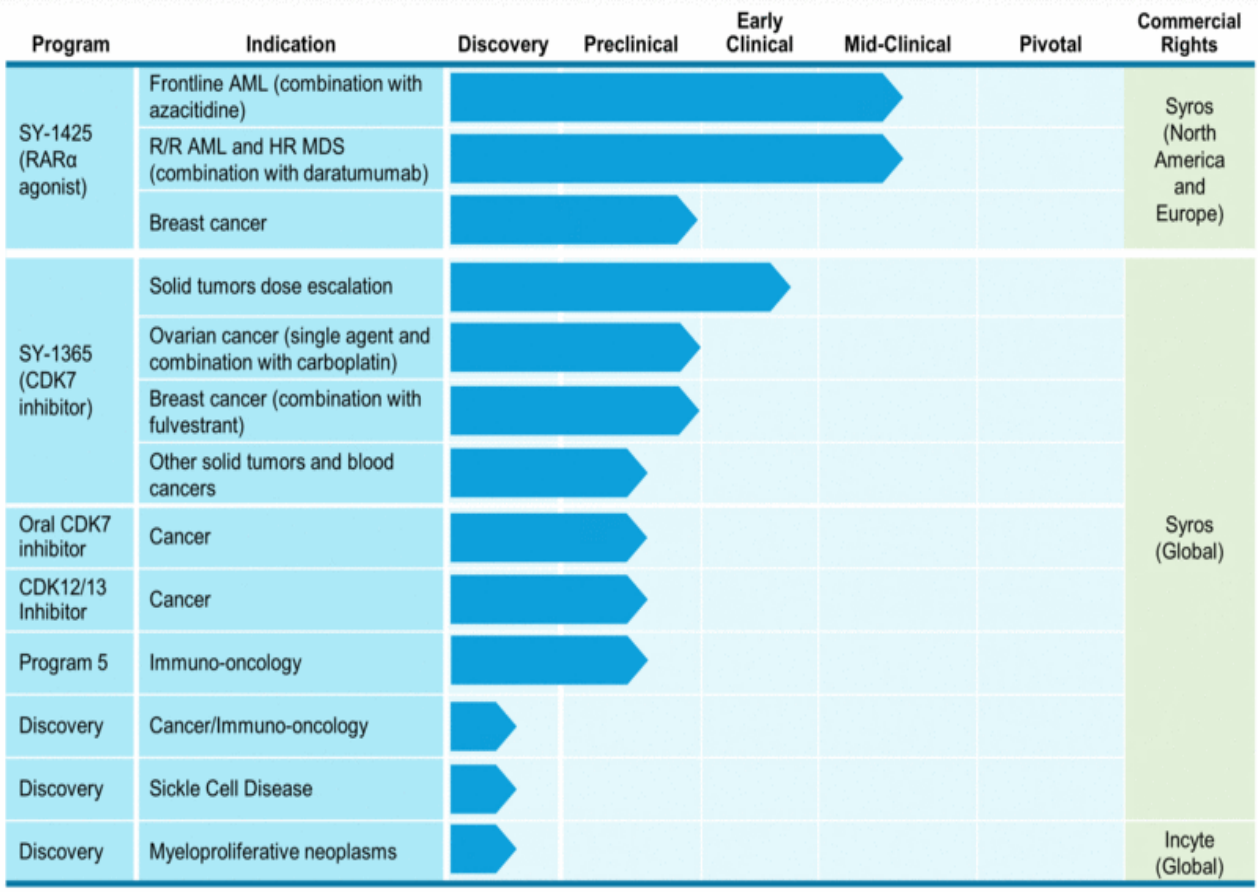
Immuno-oncology

- Modulate tumor cells, macrophages and T cells to promote tumor killing

Monogenic diseases

- Target regulatory elements to modulate expression of known gene

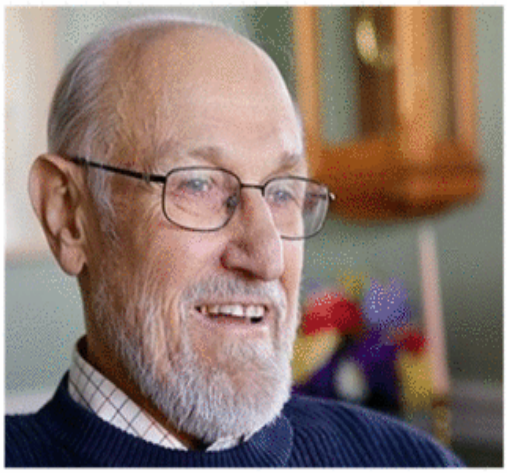
Growing pipeline with multiple potential first-in-class programs



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

SY-1425 (RARα agonist): Turning on differentiation genes in cancer

Acute Myelogenous Leukemia (AML) and Myelodysplastic Syndromes (MDS)



- First-in-class selective, oral RARα agonist
- Novel AML and MDS subsets and biomarkers discovered by Syros
- In Phase 2 trial in combination with azacitidine and daratumumab
  - Data expected in fourth quarter of 2018
  - Single-agent activity and myeloid differentiation in biomarker-positive AML and MDS patients support ongoing development in combination
  - Chronic, daily dosing generally well-tolerated as single agent
- Significant market potential
  - AML and MDS continue to be areas of high unmet need
    - Few options for newly diagnosed, unfit AML and R/R AML and HR MDS
  - Potential in additional AML and HR MDS populations and other *RARA*-positive cancers, including breast

SYROS

Ongoing Phase 2 trial evaluating SY-1425 combinations in genomically defined AML and MDS patients

- All patients selected based on *RARA* and *IRF8* biomarkers
- Two distinct combinations in difficult-to-treat AML and MDS populations
- Expect to report clinical data on both combinations in fourth quarter of 2018

Phase 2 Clinical Trial Design

SY-1425 in combination with azacitidine in newly diagnosed, unfit AML *(25 patients)*

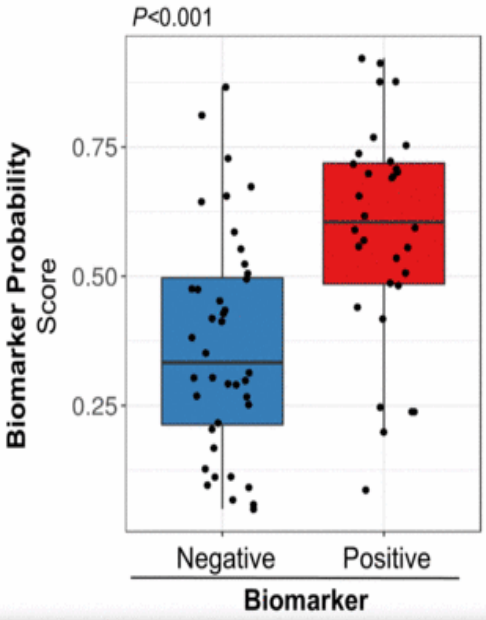
SY-1425 in combination with daratumumab in R/R AML and higher-risk MDS *(12-patient pilot)*

Endpoints

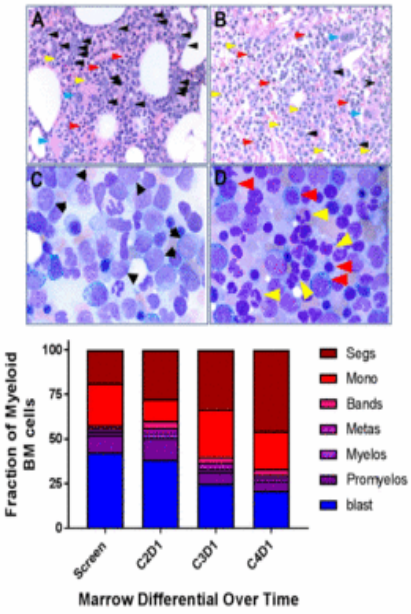
- Overall Response Rate
- Duration of Response
- Hematologic Improvement
- Safety and tolerability
- CD38 induction (daratumumab arm only)

Differentiation seen in biomarker-positive patient samples and clinical trial patients treated with single-agent SY-1425

Unbiased machine learning approach using Random-Forest analysis



66-year-old male with R/R AML



Myeloid differentiation starting after one cycle, with marrow blast reduction >25% beginning after two cycles and continuing to the start of the fourth cycle

ESH EUROPEAN SCHOOL OF HAEMATOLOGY

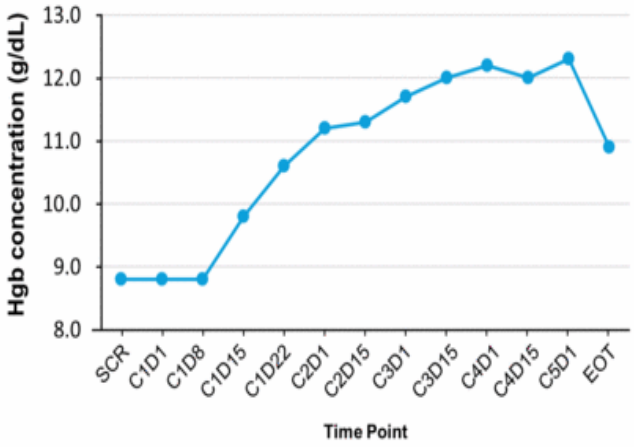
"Novel RARA Pathway Activation Biomarkers in Study SY-1425-201 Define a New Subset of AML and MDS Patients and Correlate with Myeloid Differentiation"

ASH 59th ASH Annual Meeting and Exposition

"Early Results from a Biomarker-Directed Phase 2 Trial of SY-1425 in Acute Myeloid Leukemia (AML) and Myelodysplastic Syndrome (MDS) Demonstrate DHRS3 Induction and Myeloid Differentiation Following SY-1425 Treatment"

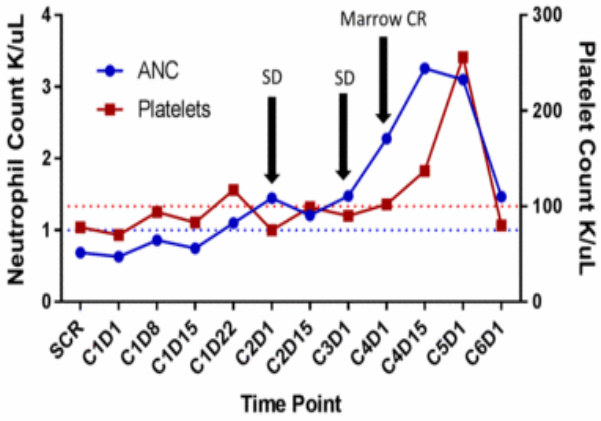
Clinical activity observed in 43% of R/R AML and HR MDS patients treated with single-agent SY-1425

Erythroid response in R/R HR MDS patient



Initial response observed two weeks after starting treatment and lasting through five months without blood transfusions

Marrow CR in R/R HR MDS patient



Initial responses (platelet and ANC) observed on cycle 1 day 22, patient remains on treatment past 238 days

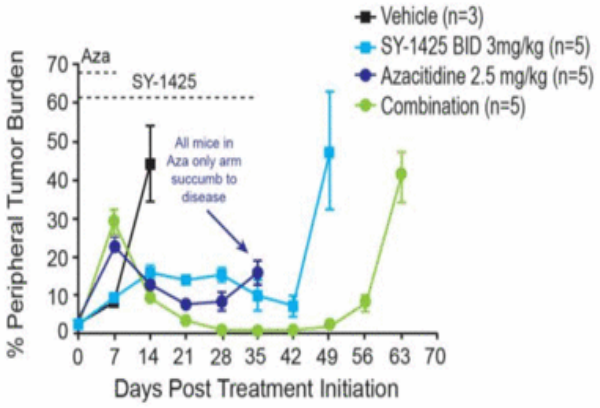
ASH 59th ASH Annual Meeting and Exposition

"Early Results from a Biomarker-Directed Phase 2 Trial of SY-1425 in Acute Myeloid Leukemia (AML) and Myelodysplastic Syndrome (MDS) Demonstrate DHRS3 Induction and Myeloid Differentiation Following SY-1425 Treatment"

SYROS

SY-1425 and AZA combination induces deeper, more durable responses and induces apoptosis preclinically

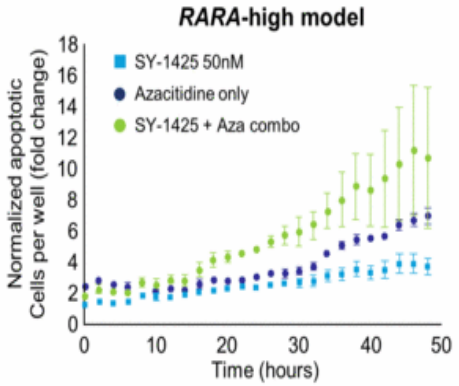
Combo leads to deeper and more durable response in preclinical PDX model

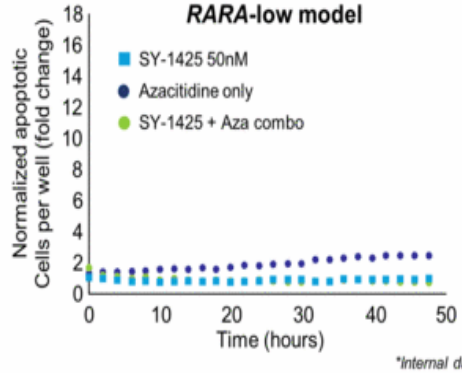


ASH 58th Annual Meeting & Exposition
San Diego, CA • December 3-6, 2016

"Clinical Pharmacodynamic Markers and Combinations with SY-1425 (tamibarotene) in a Genomically-Defined subset of non-APL AML"

Combo induces apoptosis in *RARA*-high cell lines*

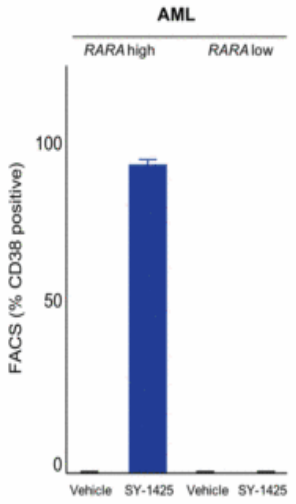




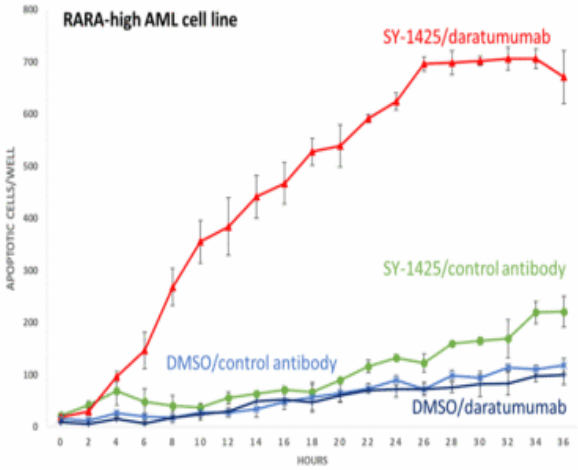
*Internal data on file

SY-1425 associated with CD38 expression preclinically and in patients; Anti-CD38 combination induces immune-mediated cell death *in vitro*

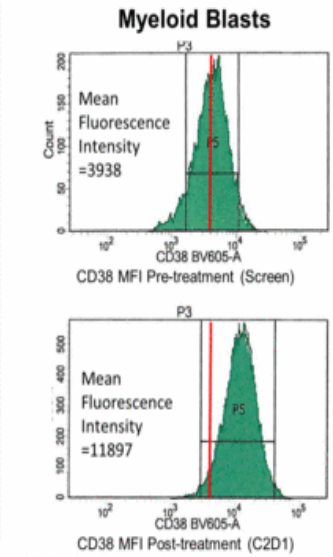
SY-1425 induces CD38 cell surface expression



SY-1425 in combination with daratumumab induces immune-mediated cell death



CD38 induction seen in 85% of evaluable clinical trial patients



AACR American Association for Cancer Research 2017

"SY-1425, a selective RARα agonist, induces high levels of CD38 expression in RARA-high AML tumors creating a susceptibility to anti-CD38 therapeutic antibody treatment"

ASH 59th ASH Annual Meeting and Exposition

"Early Results from a Biomarker-Directed Phase 2 Trial of SY-1425 in Acute Myeloid Leukemia (AML) and Myelodysplastic Syndrome (MDS) Demonstrate DHRS3 Induction and Myeloid Differentiation Following SY-1425 Treatment"

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

AML incidence[1]: ~33,000

~ 33% *RARA or IRF8* biomarker positive

HR MDS incidence[1]: ~7,500

~ 33% *RARA or IRF8* biomarker positive

Newly diagnosed, unfit

- >50% of AML patients ineligible for standard chemo upon diagnosis
- HMAs/ less intensive therapies with modest efficacy are standard-of-care
- Survival of ≤ 12 months

Newly diagnosed higher-risk

- Most patients treated with HMAs/ less intensive therapies that have modest efficacy
- Survival of 0.8-1.6 years

Relapsed or refractory

- Newly approved agents target limited subsets of patients with modest efficacy
- Patients progress quickly in relapsed setting
- Survival of < 6 months

Relapsed or refractory higher-risk

- Few treatment options with limited efficacy
- No new drugs approved since 2006
- Survival of < 6 months

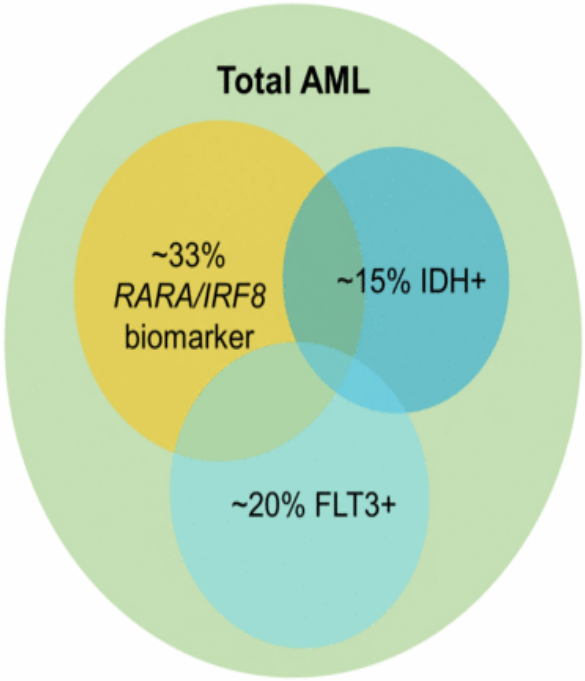
[1] Incidence figures include annual diagnoses in the U.S., Canada and the EU 5 (UK, Germany, France, Spain and Italy). Health Advances analysis.

Sources: Expert Rev. Pharmacoecon. Outcomes Res. Early online, 1–10 (2015); Clinical Lymphoma, Myeloma & Leukemia, Vol. 16, No. 11, 625-36; Blood 2012 120:2454-2465. NCCN Guidelines 2017 MDS.

SYROS

Unique mechanism and tolerability profile support broad combination potential

- Potential for combinations with chemo and targeted agents without anticipated overlapping toxicities
- *RARA and IRF8* biomarkers and SY-1425 opportunity cut across mutational landscape



Estimated frequency of *RARA/IRF8* biomarkers based on Syros' analysis of screed patients in ongoing trial, and estimated frequency of IDH and FLT3 mutations based on published studies

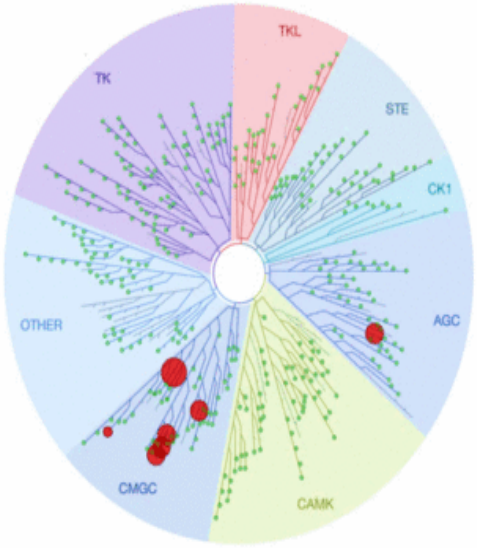
SY-1365 (CDK7 inhibitor): Controlling expression of tumor-driving genes

Difficult-to-treat solid tumors and blood cancers

- First-in-class selective inhibitor of CDK7
- Lowers expression of key tumor-driving genes, transcription factors and anti-apoptotic proteins
- CDK7 inhibition induces apoptosis and preferentially kills cancer cells over non-cancerous cells
- Currently in Phase 1 clinical trial with planned expansion into ovarian and breast cancers
  - Data from dose escalation phase expected in fourth quarter of 2018
- Broad potential to expand into additional solid tumors and blood cancers

SY-1365 is a first-in-class potent and selective CDK7 inhibitor

DiscoveRx kinome scan at 1μM SY-1365



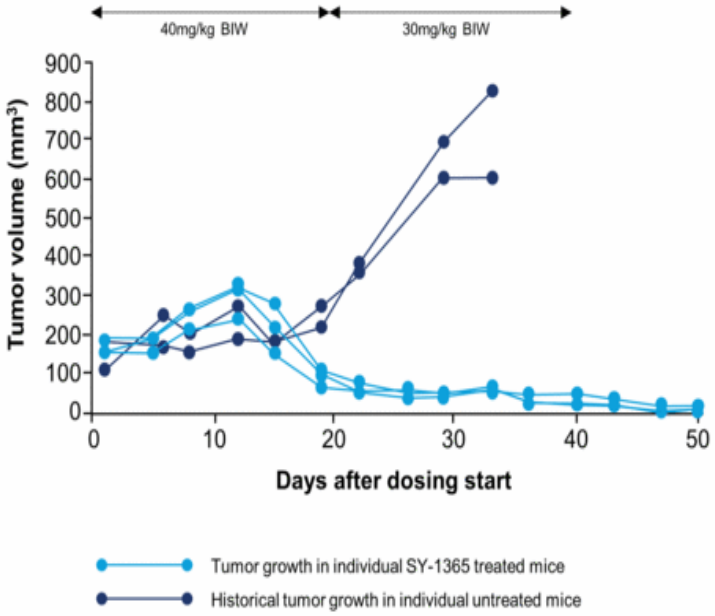
- Covalent
- Highly potent
  - Enzymatic IC50 = 22 nM
  - Cellular IC50 < 20 nM
- Highly selective
  - Greater than 30-fold selective for CDK7 over CDK9 and CDK2
  - Only binds to 7 out of 468 kinases screened at >90% binding
- Sustained PD effect (~3-day half-life)
- Durable tumor regressions in *in vivo* models using intermittent dosing regimen

AACR · NIH National Cancer Institute · EORTC

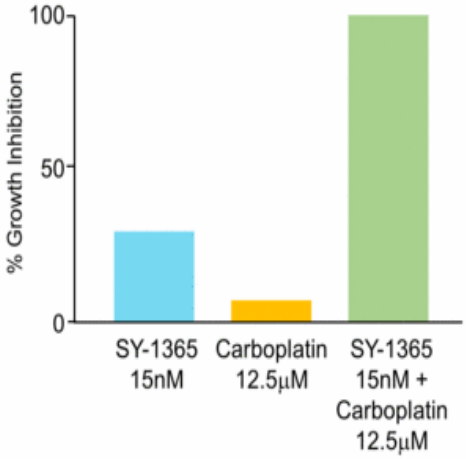
"PK/PD modeling of the first-in-class, potent and selective covalent CDK7 inhibitor, SY-1365, provides mechanistic basis for intermittent dosing regimens in preclinical efficacy models of hematological and solid tumors"

SY-1365 shows anti-tumor activity as single agent and in combination with standard-of-care in ovarian models

Chemo-relapsed ovarian cancer PDX model



Combination with carboplatin

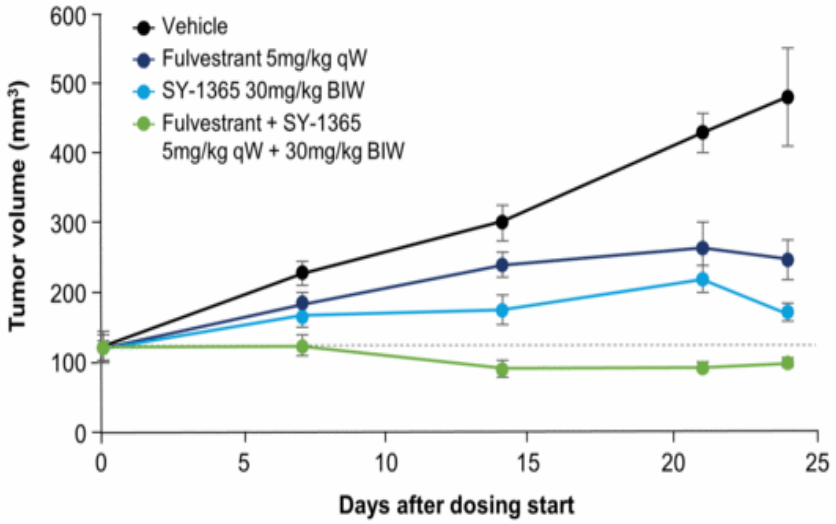


- Similar combination effect is seen with oxaliplatin and taxol in several ovarian cancer cell lines

Internal data on file

SY-1365 in combination with hormone therapy shows anti-tumor activity in HR+ breast cancer models

Hormone receptor-positive (HR+) cell-derived xenograft model



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

Source: Dana-Farber Cancer Institute

Dose escalation ongoing in Phase 1 clinical trial of SY-1365; Expansion to initially focus on ovarian and breast cancers

Phase 1 clinical trial design

Dose escalation
Open to all patients with advanced solid tumors
Exploring once and twice a week dosing

- Relapsed ovarian cancer, 3+ prior lines
  Single agent (N=24)
- Relapsed ovarian cancer, 1+ prior lines (platinum sensitive)
  Combination with carboplatin (N=24)
- Primary platinum refractory ovarian cancer
  Single agent pilot (N=12)
- HR+ metastatic breast cancer, CDK4/6 inhibitor resistant
  Combination with fulvestrant (N=12)
- Solid tumors accessible for biopsy
  Single agent (N=10)

- Expect to present data from dose escalation phase of trial in fourth quarter of 2018
  - Safety, PK/PD, proof-of-mechanism
- Expansion to study SY-1365 in multiple populations as single and combination agent
- Sets stage for expansion into additional tumor types

Significant need for new therapies in advanced high-grade serous ovarian and HR+ metastatic breast cancer

Ovarian Cancer ~59,000[1]

- 70% have high-grade serous ovarian cancer and most present with advanced disease at initial diagnosis
- Standard-of-care includes platinum-based chemotherapy as foundation
  - Majority of patients, even those who initially respond to platinum-based chemotherapy, relapse within a year
- Significant unmet need and/or limited treatment options in platinum sensitive, resistant and refractory patients

Breast Cancer ~266,000[2]

- ~80% are HR+ breast cancer
- Standard-of-care for metastatic HR+ breast cancer includes CDK4/6 inhibitor plus an aromatase inhibitor
  - ~50% of patients progress within ~2 years
- Second-line hormone-based therapies have limited efficacy, creating a need for new therapies

1 Annual ovarian cancer diagnoses in the U.S., Canada, Japan and the EU 5 (UK, Germany, France, Spain and Italy). Health Advances analysis.

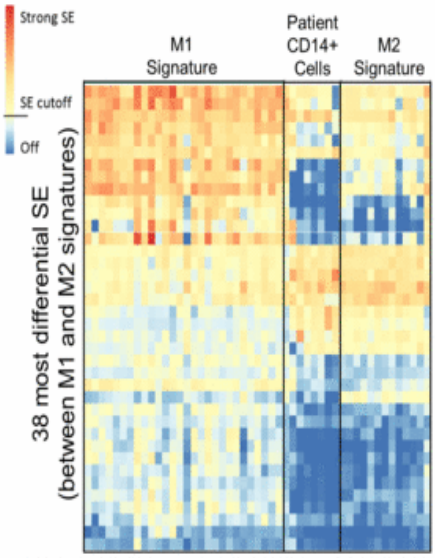
2 American Cancer Society estimate of new cases diagnosed in U.S. in 2018

Sources: Hanker et al. Ann Oncol. 2012 Oct;23(10):2605-12. SEER, Cancer Research UK 2013. NCCN Guidelines Nov. 2017. McCluggage WG. Pathology 2011; 43: 420–432. Gabra H. EJC Suppl. 2014 Dec;12(2):2-6. and Herzog TJ and Monk BJ. Onitilo AA et al., Clin Med Res 2009; 7(1-2):4-13. Rugo HS et al., JCO 2016; 34: 3069-3103. Finn RS et al, N Engl J Med 2016; 375(20): 1925-1936. Faslodex USPI

Immuno-oncology strategy: Modulate tumor and immune cells to pro-inflammatory state to promote tumor killing

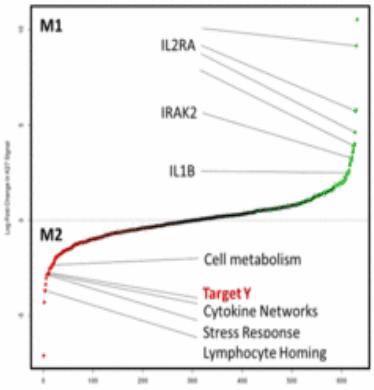
- Analyzed regulatory genomes of tumor and immune cells (breast, ovarian, pancreatic, colorectal, glioblastoma)
- Small molecule inhibitor that switches macrophages to pro-inflammatory state in preclinical studies
- Identified additional targets on tumor and immune cells for modulation

Super-enhancer signatures of M1 and M2 macrophages give insight into the functional state of CD14+ cells



"Characterizing the Epigenetic Landscape Identifies Putative Therapeutic Targets in the Pancreatic Cancer Chimera"

Small molecule inhibitor switches immunosuppressive macrophages to pro-inflammatory state



Immune cell type	Change IFNγ
CD14 naive	--
CD14 naïve*	21x
M1*	61x
M2*	6x
M2 + inhibitor*	61x

*denotes addition of activated CD8 cells

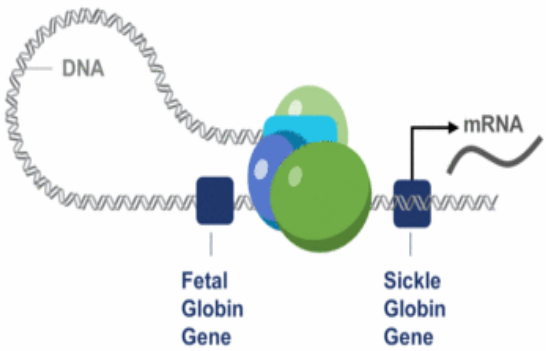
SYROS

Monogenic disease strategy: Extending our platform to alter expression of a single gene for therapeutic benefit

Sickle Cell Disease (SCD)

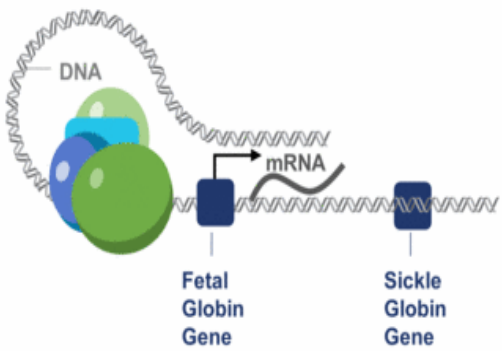
Clinical and genetic data point to therapeutic benefit of elevated fetal globin

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



Using transcriptional chemistry platform to control globin expression

- Developed detailed maps of globin expression in fetal and adult states
- Identifying gene regulatory interactions at the globin locus
- Targeting transcriptional regulators at the globin genes

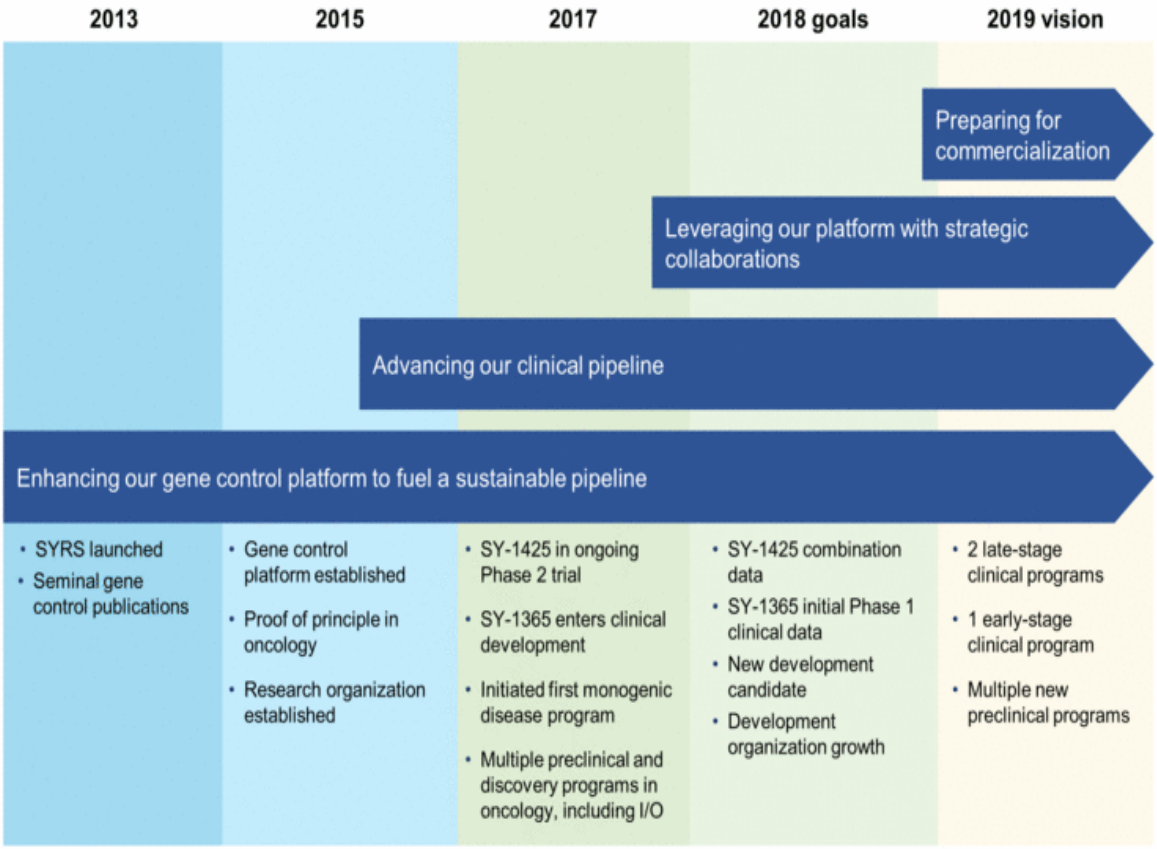


SYROS

Investment balanced across clinical pipeline and discovery to achieve short- and long-term goals

- Drive SY-1425 and SY-1365 to key value creating milestones
- Maintain investment in discovery with goal to:
  - Deliver one IND every other year on average
  - Build on leadership in gene control
- Cash runway to fund planned operations into 2020

Rapidly advancing toward our vision



www.syros.com