UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

FORM 10-Q

(Mark One)

☒ QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the quarterly period ended September 30, 2018

OR

☐ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

Commission file number: 001-37813

SYROS PHARMACEUTICALS, INC.
(Exact Name of Registrant as Specified in Its Charter)

Delaware **(State or Other Jurisdiction of Incorporation or Organization)**	**45-3772460** **(I.R.S. Employer Identification No.)**
620 Memorial Drive, Suite 300 **Cambridge, Massachusetts** **(Address of Principal Executive Offices)**	**02139** **(Zip Code)**

(617) 744-1340
(Registrant's Telephone Number, Including Area Code)

(Former Name, Former Address and Former Fiscal Year, if Changed Since Last Report)

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer ☐	Accelerated filer ☒
Non-accelerated filer ☐	Smaller reporting company ☒ 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. ☒

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

Number of shares of the registrant's common stock, $0.001 par value, outstanding on October 26, 2018: 33,654,604

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Cautionary Note Regarding Forward-Looking Statements

This Quarterly Report on Form 10-Q, or Quarterly Report, contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Quarterly Report, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management and expected market growth are forward-looking statements. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. The forward-looking statements and opinions contained in this Quarterly Report are based upon information available to us as of the date of this Quarterly Report and, while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information.

These forward-looking statements include, among other things, statements about:

- developments relating to our competitors and our industry;
- the impact of government laws and regulations;
- our plans to initiate and expand clinical trials of our product candidates and our expectations for the timing and quantity of information to be reported from our clinical trials of SY-1425 and SY-1365;
- our plans to progress SY-5609 into and through investigational new drug-enabling studies;
- planned clinical trials for our product candidates, whether conducted by us or by any future collaborators, including the timing of these trials and of the anticipated results;
- our plans to research, develop, manufacture and commercialize our current and future product candidates;
- our plans to develop and seek approval of companion diagnostic tests for use in identifying patients who may benefit from treatment with our products and product candidates;
- our expectations regarding the potential benefits of our gene control platform and our approach;
- our ability to enter into, and the terms and timing of, any collaborations, license agreements, or other arrangements;
- whether our collaboration with Incyte Corporation, or Incyte, will yield any validated targets, whether Incyte will exercise any of its options to exclusively license intellectual property directed to such targets, and whether and when any of the target validation fees, option exercise fees, milestone payments or royalties under the Incyte collaboration will ever be paid;
- the potential benefits of any future collaboration;
- the timing of and our ability to obtain and maintain regulatory approvals for our product candidates;
- the rate and degree of market acceptance and clinical utility of any products for which we receive marketing approval;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position and strategy;
- our ability to identify additional products or product candidates with significant commercial potential;
- our expectations related to the use of our current cash, cash equivalents and marketable securities and the period of time in which such capital will be sufficient to fund our planned operations; and
- our estimates regarding expenses, future revenue, capital requirements and need for additional financing.

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 the forward-looking statements we make. New risks and uncertainties emerge from time to time, and it is not possible for us to predict all risks and uncertainties that could have an impact on the forward-looking statements contained in this Quarterly Report. We have included important factors in the cautionary statements included in this Quarterly Report, particularly in the "Risk Factors" section, that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, collaborations, joint ventures or investments that we may make or enter into. You should read this Quarterly Report completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

PART I – FINANCIAL INFORMATION

Item 1. Financial Statements (unaudited)

SYROS PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(in thousands, except share and per share data)
(unaudited)

	September 30, 2018	December 31, 2017
Assets		
Current assets:		
Cash and cash equivalents	$ 43,524	$ 32,205
Marketable securities	69,707	39,844
Prepaid expenses and other current assets	1,675	917
Restricted cash, current portion	638	193
Total current assets	115,544	73,159
Property and equipment, net	3,908	3,938
Other long-term assets	892	1,101
Restricted cash, net of current portion	290	290
Total assets	$ 120,634	$ 78,488
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 2,671	$ 2,283
Accrued expenses	11,159	9,728
Deferred revenue, current portion	7,075	—
Deferred rent, current portion	383	355
Capital lease obligations, current portion	9	47
Total current liabilities	21,297	12,413
Deferred rent, net of current portion	456	745
Deferred revenue, net of current portion	4,020	—
Capital lease obligations, net of current portion	24	6
Commitments and contingencies (Note 8)		
Stockholders' equity:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized at September 30, 2018 and December 31, 2017; 0 shares issued and outstanding at September 30, 2018 and December 31, 2017	—	—
Common stock, $0.001 par value; 200,000,000 shares authorized at September 30, 2018 and December 31, 2017; 33,654,485 and 26,423,375 shares issued and outstanding at September 30, 2018 and December 31, 2017, respectively	34	26
Additional paid-in capital	294,329	220,606
Accumulated other comprehensive loss	(13)	(42)
Accumulated deficit	(199,513)	(155,266)
Total stockholders' equity	94,837	65,324
Total liabilities and stockholders' equity	$ 120,634	$ 78,488

See accompanying notes to unaudited condensed consolidated financial statements.

SYROS PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
(in thousands, except share and per share data)
(unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
Revenue	$ 412	$ —	$ 1,157	$ 1,101
Operating expenses:				
Research and development	12,856	10,447	35,054	30,116
General and administrative	3,876	3,593	11,792	10,151
Total operating expenses	16,732	14,040	46,846	40,267
Loss from operations	(16,320)	(14,040)	(45,689)	(39,166)
Other income, net	583	215	1,442	458
Net loss	$ (15,737)	$ (13,825)	$ (44,247)	$ (38,708)
Net loss per share - basic and diluted	$ (0.47)	$ (0.53)	$ (1.37)	$ (1.54)
Weighted-average number of common shares used in net loss per share - basic and diluted	33,653,479	26,259,216	32,306,261	25,100,278

See accompanying notes to unaudited condensed consolidated financial statements.

SYROS PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(in thousands)
(unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
Net loss	$(15,737)	$(13,825)	$(44,247)	$(38,708)
Other comprehensive (loss) gain:				
Unrealized holding (losses) gains on marketable securities	(6)	(4)	29	(1)
Comprehensive loss	$(15,743)	$(13,829)	$(44,218)	$(38,709)

See accompanying notes to unaudited condensed consolidated financial statements.

SYROS PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)
(unaudited)

	Nine Months Ended September 30,	
	2018	2017 (As Adjusted)
Operating activities		
Net loss	$ (44,247)	$ (38,708)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	1,172	1,137
Stock-based compensation expense	4,977	3,148
Net amortization of premiums and discounts on marketable securities	(334)	(27)
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(758)	22
Accounts receivable	—	867
Other long-term assets	(45)	(370)
Accounts payable	369	(295)
Accrued expenses	1,529	849
Deferred revenue	11,095	(550)
Deferred rent and lease incentive	(261)	(235)
Net cash used in operating activities	(26,503)	(34,162)
Investing activities		
Purchases of property and equipment	(1,189)	(754)
Proceeds from the disposition of property and equipment	9	—
Purchases of marketable securities	(72,000)	(41,768)
Maturities of marketable securities	42,500	27,000
Net cash used in investing activities	(30,680)	(15,522)
Financing activities		
Payments on capital lease obligations	(48)	(125)
Proceeds from issuance of common stock through employee benefit plans	487	918
Proceeds from issuance of common stock in public offerings and private placements, net of issuance costs	68,508	32,452
Net cash provided by financing activities	68,947	33,245
Increase (decrease) in cash, cash equivalents and restricted cash	11,764	(16,439)
Cash, cash equivalents and restricted cash		
Beginning of period	32,688	59,071 *
End of period	$ 44,452	$ 42,632 *
Supplemental disclosure of cash flow information:		
Cash paid for interest	$ 1	$ 8
Non-cash investing and financing activities		
Property and equipment received but unpaid as of period end	$ 77	$ 9
Assets acquired under capital lease	$ 28	$ —
Offering costs incurred but unpaid as of period end	$ —	$ 60

* Recast to reflect adoption of Accounting Standard Update 2016-18 Restricted Cash - Refer to Note 6

See accompanying notes to unaudited condensed consolidated financial statements.

1. Nature of Business

Syros Pharmaceuticals, Inc. (the "Company"), a Delaware corporation formed in November 2011, is a biopharmaceutical company pioneering an understanding of the non-coding regulatory region of the genome to advance a new wave of medicines that control the expression of genes.

The Company is subject to a number of risks similar to those of other early stage companies, including dependence on key individuals; risks inherent in the development and commercialization of medicines to treat human disease; competition from other companies, many of which are larger and better capitalized; risks relating to obtaining and maintaining necessary intellectual property protection; and the need to obtain adequate additional financing to fund the development of its product candidates and discovery activities. If the Company is unable to raise capital when needed or on favorable terms, it would be forced to delay, reduce, eliminate or out-license certain of its research and development programs or future commercialization rights to its product candidates.

During the nine months ended September 30, 2018, the Company issued and sold an aggregate of 1,373,677 shares of its common stock to the public pursuant to its at-the-market sales facility, resulting in aggregate proceeds of $16.6 million. In February 2018, the Company issued and sold an aggregate of 4,188,481 shares of its common stock in a public offering at a price of $9.55 per share, resulting in gross proceeds of $40.0 million before deducting underwriting commissions and fees of approximately $3.0 million. The underwriters exercised their option to purchase an additional 628,272 shares at a price per share of $9.55, resulting in additional gross proceeds of $6.0 million before deducting underwriting commissions and fees of approximately $0.4 million. In February 2018, the Company also completed a private placement of 144,505 shares of common stock to Incyte Corporation (“Incyte”), for aggregate proceeds of $1.4 million. In January 2018, the Company completed a private placement of 793,021 shares of common stock to Incyte for aggregate proceeds of $10.0 million in connection with entry into a target discovery collaboration with Incyte (refer to Note 3).

The Company has incurred significant annual net operating losses in every year since its inception. It expects to continue to incur significant and increasing net operating losses for at least the next several years. The Company’s net losses were $54.0 million, $47.7 million and $29.8 million for the years ended December 31, 2017, 2016 and 2015, respectively, and $44.2 million for the nine months ended September 30, 2018. As of September 30, 2018, the Company had an accumulated deficit of $199.5 million. The Company has not generated any revenues from product sales, has not completed the development of any product candidate and may never have a product candidate approved for commercialization. The Company has financed its operations to date primarily through the sale of equity securities. The Company has devoted substantially all of its financial resources and efforts to research and development and general and administrative expense to support such research and development. The Company’s net losses may fluctuate significantly from quarter to quarter and year to year. Net losses and negative cash flows have had, and will continue to have, an adverse effect on the Company’s stockholders' equity and working capital. The Company believes that its cash, cash equivalents and marketable securities of $113.2 million as of September 30, 2018, will be sufficient to allow the Company to fund its current operating plan for a period of at least 12 months past the issuance date of these unaudited interim condensed consolidated financial statements.

2. Summary of Significant Accounting Policies

Basis of Presentation

The Company’s unaudited interim condensed consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States (“U.S. GAAP”). Any reference in these notes to applicable guidance is meant to refer to the authoritative U.S. GAAP as found in the Accounting Standards Codification (“ASC”) and Accounting Standards Updates (“ASU”) of the Financial Accounting Standards Board (“FASB”). Certain information and footnote disclosures normally included in financial statements prepared in accordance with U.S. GAAP have been condensed or omitted from this report, as is permitted by such rules and regulations. Accordingly, these financial statements should be read in conjunction with the financial statements as of and for the year ended December 31, 2017 and notes thereto included in the Company’s Annual Report on Form 10-K for the year ended December 31, 2017 filed with the Securities and Exchange Commission (“SEC”) on March 12, 2018.

The unaudited interim condensed consolidated financial statements have been prepared on the same basis as the audited financial statements except as noted below with respect to the adoption of ASC Topic 606, *Revenue from Contracts with Customers* ("Topic 606"). In the opinion of the Company's management, the accompanying unaudited interim condensed consolidated financial statements contain all adjustments that are necessary to present fairly the Company's financial position as of September 30, 2018, the results of its operations for the three and nine months ended September 30, 2018 and 2017, and cash flows for the nine months ended September 30, 2018 and 2017. Such adjustments are of a normal and recurring nature. The results for the three and nine months ended September 30, 2018 are not necessarily indicative of the results for the year ending December 31, 2018, or for any future period.

Principles of Consolidation

The accompanying condensed consolidated financial statements include the accounts of Syros Pharmaceuticals, Inc. and its wholly owned subsidiary, Syros Securities Corporation, which is a Massachusetts corporation formed by the Company in December 2014 to exclusively engage in buying, selling and holding securities on its own behalf. All intercompany transactions and balances have been eliminated in consolidation.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts in the financial statements and accompanying notes. Management considers many factors in selecting appropriate financial accounting policies and in developing the estimates and assumptions that are used in the preparation of the financial statements. Management must apply significant judgment in this process. In addition, other factors may affect estimates, which include, but are not limited to, expected business and operational changes, sensitivity and volatility associated with the assumptions used in developing estimates and whether historical trends are expected to be representative of future trends. Management's estimation process often may yield a range of potentially reasonable estimates and management must select an amount that falls within that range of reasonable estimates. On an ongoing basis, the Company's management evaluates its estimates, which include, but are not limited to, estimates related to revenue recognition, stock-based compensation expense, accrued expenses and income taxes. Actual results may differ from those estimates or assumptions.

Segment Information

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker, or decision-making group, in making decisions on how to allocate resources and assess performance. The Company's chief operating decision maker is the Chief Executive Officer. The Company and the chief operating decision maker view the Company's operations and manage its business in one operating segment. The Company operates only in the United States.

Cash and Cash Equivalents

The Company considers all highly liquid instruments that have original maturities of three months or less when acquired to be cash equivalents. Cash equivalents, which consist of money market funds that invest in U.S. Treasury obligations, as well as overnight repurchase agreements, are stated at fair value. The Company maintains its bank accounts at one major financial institution.

Fair Value of Financial Instruments

ASC 820, *Fair Value Measurement* ("ASC 820"), established a fair value hierarchy for instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company's own assumptions (unobservable inputs). Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumption about the inputs that market participants would use in pricing the asset or liability, and are developed based on the best information available in the circumstances.

ASC 820 identified fair value as the exchange price, or exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As a basis for

considering market participant assumptions in fair value measurements, ASC 820 established a three-tier fair value hierarchy that distinguishes between the following:

Level 1—Quoted market prices (unadjusted) in active markets for identical assets or liabilities.

Level 2—Inputs other than quoted prices included within Level 1 that are either directly or indirectly observable, such as quoted market prices, interest rates and yield curves.

Level 3—Unobservable inputs developed using estimates or assumptions developed by the Company, which reflect those that a market participant would use.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized as Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

The carrying amounts reflected in the condensed consolidated balance sheets for cash and cash equivalents, prepaid expenses, other current assets, accounts payable, accrued expenses and deferred revenue approximate their fair values, due to their short-term nature.

Revenue Recognition

To date the Company's only revenue has consisted of collaboration and license revenue. The Company has not generated any revenue from product sales and does not expect to generate any revenue from product sales for the foreseeable future. For the three and nine months ended September 30, 2018, the Company recognized approximately $0.4 million and $1.2 million of revenue, respectively, all of which was attributable to its target discovery collaboration with Incyte. For the nine months ended September 30, 2017, the Company recognized $1.1 million of revenue, all of which was attributable to a research agreement with a multinational pharmaceutical company that expired in accordance with its terms in March 2017. No revenue was recognized for the three months ended September 30, 2017.

On January 1, 2018, the Company adopted Topic 606 using the modified retrospective method and applied the new standard to contracts that have been not completed as of the January 1, 2018 adoption date. As of the January 1, 2018 adoption date, the Company did not have any contracts that were not yet completed.

Topic 606 applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments. Under Topic 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of Topic 606, the entity performs the following five steps:

(i) identify the contract(s) with a customer;

(ii) identify the performance obligations in the contract;

(iii) determine the transaction price;

(iv) allocate the transaction price to the performance obligations in the contract; and

(v) recognize revenue when (or as) the entity satisfies a performance obligation.

The Company only applies the five-step model to contracts when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of Topic 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations, and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

The Company from time to time enters into agreements that are within the scope of Topic 606. The terms of these arrangements typically include payment to the Company of one or more of the following: non-refundable, up-front license fees; development, regulatory and commercial milestone payments; and royalties on net sales of licensed products. Each of these payments results in license and collaboration revenues, except for revenues from royalties on net sales of licensed products, which will be classified as royalty revenues.

The Company analyzes its collaboration arrangements to assess whether they are within the scope of ASC 808, *Collaborative Arrangements* ("ASC 808"), to determine whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities. This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For collaboration arrangements within the scope of ASC 808 that contain multiple elements, the Company first determines which elements of the collaboration are deemed to be within the scope of ASC 808 and those that are more reflective of a vendor-customer relationship and therefore within the scope of Topic 606. For elements of collaboration arrangements that are accounted for pursuant to ASC 808, an appropriate recognition method is determined and applied consistently, generally by analogy to Topic 606. For those elements of the arrangement that are accounted for pursuant to Topic 606, the Company applies the five-step model described above.

Research and Development

Expenditures relating to research and development are expensed in the period incurred. Research and development expenses consist of both internal and external costs associated with the development of the Company's gene control platform and product candidates. Research and development costs include salaries and benefits, materials and supplies, external research, preclinical and clinical development expenses, stock-based compensation expense and facilities costs. Facilities costs primarily include the allocation of rent, utilities, depreciation and amortization.

In certain circumstances, the Company is required to make nonrefundable advance payments to vendors for goods or services that will be received in the future for use in research and development activities. In such circumstances, the nonrefundable advance payments are deferred and capitalized, even when there is no alternative future use for the research and development, until related goods or services are provided.

The Company records accruals for estimated ongoing research costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the work being performed, including the phase or completion of the event, invoices received and costs. Significant judgements and estimates may be made in determining the accrued balances at the end of any reporting period. Actual results could differ from the Company's estimates.

The Company may in-license the rights to develop and commercialize product candidates. For each in-license transaction the Company evaluates whether it has acquired processes or activities along with inputs that would be sufficient to constitute a "business" as defined under U.S. GAAP. A "business" as defined under U.S. GAAP consists of inputs and processes applied to those inputs that have the ability to create outputs. Although businesses usually have outputs, outputs are not required for an integrated set of activities to qualify as a business. When the Company determines that it has not acquired sufficient processes or activities to constitute a business, any up-front payments, as well as milestone payments, are immediately expensed as acquired research and development in the period in which they are incurred.

Stock-Based Compensation Expense

The Company accounts for its stock-based compensation awards in accordance with ASC 718, *Compensation—Stock Compensation* ("ASC 718"). ASC 718 requires all stock-based payments to employees and directors, including grants of restricted stock and stock options, to be recognized as expense in the consolidated statements of operations based on their grant date fair values. Grants of restricted stock and stock options to other service providers, referred to as non-employees, are required to be recognized as expense in the consolidated statements of operations based on their vesting date fair values. The Company estimates the fair value of options granted using the Black-Scholes option-pricing model. Prior to June 30, 2016, the Company was a private company and, therefore, lacks Company-specific historical and implied volatility information. As a result, it estimates its expected stock volatility based on the historical volatility of a publicly traded set of peer companies and expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded stock price. The expected term of the Company's stock options has been

determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. The expected term of stock options granted to non-employees is equal to the contractual term of the option award. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that the Company has never paid cash dividends and does not expect to pay any cash dividends in the foreseeable future. The Company uses the value of its common stock to determine the fair value of restricted stock awards.

The amount of stock-based compensation expense recognized during a period is based on the fair value of the portion of the awards that are ultimately expected to vest. The Company accounts for forfeitures as they occur instead of estimating forfeitures at the time of grant. Ultimately, the actual expense recognized over the vesting period will be for only those options that vest.

The Company expenses the fair value of its stock-based awards to employees on a straight-line basis over the associated service period, which is generally the vesting period. For stock-based awards granted to non-employees, stock-based compensation expense is recognized over the period during which services are rendered by such non-employees until completed. At the end of each financial reporting period prior to completion of the service, the fair value of these awards is remeasured using the then-current fair value of such awards.

For stock-based awards that contain performance-based milestones, the Company records stock-based compensation expense in accordance with the accelerated attribution model. Management evaluates when the achievement of a performance-based milestone is probable based on the expected satisfaction of the performance conditions as of the reporting date. For certain of the Company's performance-based awards, notwithstanding any vesting in accordance with the achievement of performance-based milestones, such awards vest in full on the sixth anniversary of the vesting commencement date.

Net Loss per Share

Basic net loss per share is calculated by dividing net loss by the weighted average shares outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share is calculated by adjusting the weighted average shares outstanding for the dilutive effect of common stock equivalents outstanding for the period, determined using the treasury-stock method and the if-converted method. For purposes of the dilutive net loss per share calculation, stock options are considered to be common stock equivalents but are excluded from the calculation of diluted net loss per share, as their effect would be anti-dilutive; therefore, basic and diluted net loss per share were the same for all periods presented as a result of the Company's net losses.

The following common stock equivalent was excluded from the calculation of diluted net loss per share for the periods indicated because including them would have had an anti-dilutive effect:

	As of September 30,	
	2018	2017
Stock options	3,711,150	2,771,115

Income Taxes

In December 2017, the SEC staff issued Staff Accounting Bulletin 118 to address the application of U.S. GAAP in situations when a registrant does not have the necessary information available, prepared, or analyzed (including computations) in reasonable detail to complete the accounting for certain income tax effects of H.R.1 (Tax Cuts and Jobs Act). The Company has recognized provisional tax impacts related to the re-valuation of deferred tax assets and liabilities and included these amounts in its consolidated financial statements for the year ended December 31, 2017. The Company has no foreign operations and, therefore, does not have an associated liability from the repatriation tax on accumulated earnings in H.R.1. The ultimate impact may differ from these provisional amounts, possibly materially, due to, among other things, additional analysis, changes in interpretations and assumptions the Company has made, additional regulatory guidance that may be issued, and actions the Company may take as a result of H.R.1. The Company's accounting treatment is expected to be complete in the fourth quarter of 2018, which is one year from the enactment of H.R.1.

Recent Accounting Pronouncements

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)* ("ASC 842"), which applies to all leases and will require lessees to record most leases on the balance sheet but recognize expense in a manner similar to the current standard. ASC 842 is effective for fiscal years beginning after December 15, 2018 and interim periods within those years and, as such, will be effective for the year ended December 31, 2019 for the Company. Entities are required to use a modified retrospective approach of adoption for leases that exist or are entered into after the beginning of the earliest comparative period in the financial statements. Full retrospective application is prohibited. The modified retrospective approach includes a number of optional practical expedients primarily focused on leases that commenced before the effective date of ASC 842, including continuing to account for leases that commence before the effective date in accordance with previous guidance, unless the lease is modified. In July 2018, the FASB issued ASU No. 2018-11, *Leases* (Topic 842): *Targeted Improvements*, which clarifies ASC 842 and provides companies with an optional transition method. The optional transition method allows for companies to adopt ASC 842 as of the January 1, 2019 adoption date and record a cumulative catch-up to related earnings during the period of adoption. The Company is currently in the process of quantifying the impact ASC 842 will have on its condensed consolidated balance sheets and statement of operations. The Company anticipates adopting the new standard using the optional transition method and only presenting the right of use asset and lease liability as of the January 1, 2019 adoption date. The Company also anticipates electing the practical expedients as part of the adoption of ASC 842 and will not reassess the classification of leases executed prior to the January 1, 2019 adoption date. While the Company continues to evaluate the provisions of ASC 842 to determine how it will be effected, the primary effect of adopting the new standard is currently expected to be the recording of a right of use asset and lease liability for the current operating lease for its office and laboratory facility as of the January 1, 2019 adoption date.

In June 2018, the FASB issued ASU No. 2018-07, *Compensation -Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting* ("ASU 2018-07"). ASU 2018-07 aims to simplify the accounting for share-based payments to nonemployees by aligning it to the accounting for share-based payments to employees including determining the fair value of the award on the date of grant and recognizing the stock-based compensation expense as of the respective vesting date. The new standard also requires companies to elect to either measure the awards to nonemployees over an estimated expected term or contractual term as well as elect to estimate forfeitures or account for forfeitures as incurred. ASU 2018-07 is effective for fiscal years and interim periods within those fiscal years beginning after December 15, 2018. Early adoption is permitted. ASU 2018-07 is to be adopted using a modified retrospective approach with a cumulative catch-up to retained earnings recorded for equity-classified awards for which a measurement date has not been established as of the date of adoption. The Company is currently in the process of evaluating the impact of ASU 2018-07, but does not anticipate ASU 2018-07 will have a material impact on its condensed consolidated financial statements and related disclosures.

In August 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurements (Topic 820* ("ASU 2018-13")*),* which provides for changes to the disclosure requirements for recurring and nonrecurring fair value measurements under Topic 820. ASU 2018-13 is effective for fiscal years and interim periods within those fiscal years beginning after December 15, 2019. Provisions of ASU 2018-13 including changes in unrealized gains and losses, the range and weighted average of significant unobservable inputs used to develop Level 3 fair value measurements, and the narrative description of measurement uncertainty are required to be applied prospectively for only the most recent interim or annual period presented in the initial fiscal year of adoption. All other amendments in ASU 2018-13 should be applied retrospectively to all periods presented upon their effective date. Early adoption is permitted upon issuance of ASU 2018-13. The Company is currently in the process of evaluating the new standard but does not anticipate ASU 2018-13 will have a material impact on its condensed consolidated financial statements and related disclosures.

Recently Adopted Accounting Pronouncements

In May 2014, the FASB issued ASU No. 2014-09, *Revenue from Contracts with Customers, (Topic 606)* ("ASU 2014-09"). ASU 2014-09 amends the guidance for the recognition of revenue from contracts with customers to transfer goods and services. The FASB subsequently issued additional, clarifying standards to address issues arising from the implementation of the new revenue recognition standard. The new revenue recognition standard and clarifying standards require an entity to recognize revenue when control of promised goods or services is transferred to the customer at an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. The Company adopted ASU 2014-09 as of January 1, 2018 and has elected to adopt ASU 2014-09 using the modified retrospective approach and applied the standard only to contracts that have not been completed as of the January 1, 2018 adoption date. As of the January 1, 2018 adoption date, the Company did not have any contracts that were not yet completed and will apply the new standard to all future contracts executed. The adoption of ASU 2014-09 did not have a material impact on the Company's condensed consolidated financial statements and related disclosures. During the nine months ended September 30, 2018, the Company entered into a target discovery collaboration with Incyte that is accounted for in accordance with Topic 606, as discussed in Note 3. During the three and nine months ended September 30, 2018, the Company recognized $0.4 million and $1.2 million of revenue, respectively, related to the target discovery collaboration, compared to $0.4 million and $1.2 million, respectively, that would have been recognized in accordance with the previous revenue recognition policies of ASC 605.

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows (Topic 230)* ("ASU 2016-15"), which simplifies certain elements of cash flow classification. The new guidance is intended to reduce diversity of practice in how certain transactions are classified in the statement of cash flows and is effective for annual periods beginning after December 15, 2017. The Company adopted ASU 2016-15 on January 1, 2018. The adoption of ASU 2016-15 did not have a material impact on the Company's condensed consolidated statement of cash flows and related disclosures.

In November 2016, the FASB issued ASU No. 2016-18, *Restricted Cash* ("ASU 2016-18"). The amendments in ASU 2016-18 require an entity to reconcile and explain the period-over-period change in total cash, cash equivalents and restricted cash within its statements of cash flows. The Company adopted ASU 2016-18 on January 1, 2018 using the full retrospective approach. As a result of the adoption of ASU 2016-18, the Company included $0.6 million and $0.5 million of restricted cash in the ending balances of cash, cash equivalents and restricted cash in the Company's condensed consolidated statement of cash flows for the nine months ended September 30, 2018 and 2017, respectively.

In January 2017, the FASB issued ASU No. 2017-01, *Business Combinations (Topic 805): Clarifying the Definition of a Business* ("ASU 2017-01"). The amended guidance clarifies the definition of a business with the objective of adding guidance to assist entities with evaluating whether transactions should be accounted for as acquisitions (or disposals) of assets or businesses. The Company adopted ASU 2017-01 on January 1, 2018 and will apply the guidance prospectively. The adoption of ASU 2017-01 did not have a material impact on the Company's condensed consolidated financial statements and related disclosures.

3. Agreements with Incyte Corporation

On January 8, 2018, the Company and Incyte entered into a Target Discovery, Research Collaboration and Option Agreement (the "Collaboration Agreement"). Under the Collaboration Agreement, the Company is using its proprietary gene control platform to identify novel therapeutic targets with a focus on myeloproliferative neoplasms, and Incyte has received options to obtain exclusive worldwide rights to intellectual property resulting from the collaboration for the development and commercialization of therapeutic products directed to up to seven validated targets. Incyte will have exclusive worldwide rights to develop and commercialize any therapies under the collaboration that modulate those validated targets.

On January 8, 2018, the Company also entered into a Stock Purchase Agreement with Incyte (the "Stock Purchase Agreement") whereby, for an aggregate purchase price of $10.0 million, Incyte purchased 793,021 shares of the Company's common stock at $12.61 per share. Under the terms of the Stock Purchase Agreement, the shares were purchased at 30% premium over the volume-weighted sale price of the shares of the Company's common stock over the fifteen (15) trading day period immediately preceding the date of the Stock Purchase Agreement.

Collaboration Agreement

Under the terms of the Collaboration Agreement, Incyte paid the Company $10.0 million in up-front consideration, consisting of $2.5 million in cash and $7.5 million in pre-paid research funding (the “Prepaid Research Amount”). The Company’s activities under the Collaboration Agreement are subject to a joint research plan and, subject to certain exceptions, Incyte is responsible for funding the Company’s activities under the research plan, including amounts in excess of the pre-paid research funding amount. Under the Collaboration Agreement, the Company is required to use commercially reasonable efforts to conduct the research services over a period commencing on the effective date of the Collaboration Agreement and ending upon the completion of specified target validation activities (the "Research Term").

The Company is eligible to receive target selection milestone payments, which extend the period of time in which the options are exercisable, and option exercise fees of up to an aggregate of $54.0 million if Incyte selects the maximum number of targets for validation and exercises its options to obtain exclusive rights to collaboration intellectual property for seven validated targets. Should any therapeutic product be developed by Incyte against a target as to which Incyte has exercised its option to obtain exclusive rights to collaboration intellectual property, the Company will be eligible to receive milestone payments and, if approved and commercialized, royalty payments from Incyte. For each of the up to seven validated targets, the Company would become eligible to receive from Incyte a total of up to $50.0 million in development and regulatory milestone payments. If products arising from the collaboration are approved, the Company would become eligible to receive from Incyte, for each validated target, a total of up to $65.0 million in commercial milestone payments. Upon approval and commercialization of any therapeutic product resulting from the collaboration, the Company would become eligible to receive low single-digit royalties on net sales of such product.

The term of the Collaboration Agreement began on January 8, 2018 and, unless terminated by a party early, will continue until all royalty obligations for products arising from the collaboration expire. The Collaboration Agreement may be terminated by Incyte for convenience on sixty (60) days’ prior written notice to the Company, or by the Company on thirty (30) days’ written notice in the event Incyte or one of its affiliates or sublicensees challenges the validity or enforceability of certain patent rights controlled by the Company. The Collaboration Agreement may also be terminated by either of the parties on thirty (30) days’ prior written notice in the event of an uncured material breach of the Collaboration Agreement by the other party or immediately in the case of certain bankruptcy events. If the Collaboration Agreement is terminated by Incyte for material breach, then the Company shall refund any unexpended Prepaid Research Amount. Incyte’s right to terminate for convenience and each party’s right to terminate for uncured material breach may be exercised either with respect to the Collaboration Agreement in its entirety or, as applicable, in relation to the relevant validated target and associated therapeutic products.

Collaboration Revenue

The Company analyzed the Collaboration Agreement to assess whether it is within the scope of ASC 808. As it was determined that the arrangement did not involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities, the Company concluded that the Collaboration Agreement was not in the scope of ASC 808. The Company assessed the Collaboration Agreement and concluded that it represents a contract with a customer within the scope of Topic 606.

The Company has identified a single performance obligation which includes a (i) research license that Incyte retains as long as there remains an unexercised option (the “Research License”) and (ii) research and development services provided during the Research Term (the “Research Services”). The Collaboration Agreement includes options to (x) obtain additional time to exercise the license options for certain targets designated as definitive validation targets and (y) obtain license rights to each validated target, both of which were not considered by the Company’s management to be material rights, and therefore not performance obligations, at inception. The Company’s management believes the options do not provide a material right to the customer that it would receive without entering into the contract principally because the option fees are at least equal to the standalone selling price for the underlying goods. The Research License is not considered distinct as Incyte cannot benefit from the Research License without the Research Services that are separately identifiable in the contract. The Research License only allows Incyte to evaluate the targets developed as part of the conduct of the Research Services under the research plan or conduct work allocated to them during the Research Term. Incyte cannot extract any benefit from the Research License without the Research Services, including the provision of data package information, performed by the Company. As such, these two promises are deemed inputs to a

combined output (the delivery of data package allowing Incyte to make an option exercise decision) and are bundled into a single performance obligation (the "Research License and Research Service Performance Obligation").

At inception, the total transaction price was determined to be $12.3 million, which consisted of a $2.5 million upfront non-refundable and non-creditable payment, the $7.5 million Prepaid Research Amount and $2.3 million in premium paid on the equity investment made pursuant the Stock Purchase Agreement. The Collaboration Agreement also provides for development and regulatory milestones that are only payable subsequent to the exercise of an option and were therefore excluded from transaction price at inception. The Company intends to re-evaluate the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur. There were no changes to the transaction price during the three and nine months ended September 30, 2018.

Topic 606 requires an entity to recognize revenue only when it satisfies a performance obligation by transferring a promised good or service to a customer. A good or service is considered to be transferred when the customer obtains control. As the Research License and Research Services represent one performance obligation, the Company has determined that it will satisfy its performance obligation over a period of time as services are performed and Incyte receives the benefit of the services, as the overall purpose of the arrangement is for the Company to perform the services.

The Company intends to recognize revenue related to the Research License and Research Services Performance Obligation as the underlying services are performed using an input measure over the period the Company expects to complete the performance obligation. The Company measures proportional performance based on an input method using actual costs incurred relative to the total estimated costs of the Research Services.

During the three and nine months ended September 30, 2018, the Company recognized revenue of approximately $0.4 million and $1.2 million, respectively, under the Collaboration Agreement. As of September 30, 2018, the Company has deferred revenue outstanding under the Collaboration Agreement of approximately $11.1 million, of which $7.1 million and $4.0 million were classified as current and long-term, respectively, on the Company's condensed consolidated balance sheets.

The following table presents the changes in the Company's deferred revenue liabilities for the nine months ended September 30, 2018 (in thousands):

Nine months ended September 30, 2018	Balance at Beginning of Period	Additions	Deductions	Balance at End of Period
Deferred revenue	$ —	$ 12,252	$ 1,157	$ 11,095

4. Cash, Cash Equivalents and Marketable Securities

Cash equivalents are highly liquid investments that are readily convertible into cash with original maturities of three months or less when purchased. Marketable securities consist of securities with original maturities greater than 90 days when purchased. The Company classifies these marketable securities as available-for-sale and records them at fair value in the accompanying condensed consolidated balance sheets. Unrealized gains or losses are included in accumulated other comprehensive loss. Premiums or discounts from par value are amortized to other income over the life of the underlying security.

Cash, cash equivalents and marketable securities consisted of the following at September 30, 2018 and December 31, 2017 (in thousands):

September 30, 2018	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Cash and Cash equivalents:				
Cash and money market funds	$ 20,524	$ —	$ —	$ 20,524
Overnight repurchase agreements	23,000	—	—	23,000
Marketable Securities:				
U.S. treasury obligations	69,720	—	(13)	69,707
Total:	$ 113,244	$ —	$ (13)	$ 113,231

December 31, 2017	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Cash and Cash equivalents:				
Cash and money market funds	$ 17,205	$ —	$ —	$ 17,205
Overnight repurchase agreements	15,000	—	—	15,000
Marketable Securities:				
U.S. treasury obligations	39,886	—	(42)	39,844
Total:	$ 72,091	$ —	$ (42)	$ 72,049

Although available to be sold to meet operating needs or otherwise, securities are generally held through maturity. The cost of securities sold is determined based on the specific identification method for purposes of recording realized gains and losses. During the three and nine months ended September 30, 2018, there were no realized gains or losses on sales of investments, and no investments were adjusted for other-than-temporary declines in fair value.

As of September 30, 2018 and December 31, 2017, all marketable securities had maturities of less than twelve months when purchased.

At September 30, 2018, the Company held fourteen securities that were in an unrealized loss position. The aggregate fair value of securities held by the Company in an unrealized loss position for less than 12 months as of September 30, 2018 was $69.7 million, and there were no securities held by the Company in an unrealized loss position for more than 12 months. The Company has the intent and ability to hold such securities until recovery. The Company determined that there was no material change in the credit risk of the above investments. As a result, the Company determined it did not hold any investments with an other-than-temporary impairment as of September 30, 2018.

5. Fair Value Measurements

Assets measured at fair value on a recurring basis as of September 30, 2018 and December 31, 2017 were as follows (in thousands):

Description	September 30, 2018	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Cash and cash equivalents:				
Cash and money market funds	$ 20,524	$ 20,524	$ —	$ —
Overnight repurchase agreements	23,000	—	23,000	—
Marketable securities:				
U.S. treasury obligations	69,707	69,707	—	—
	$ 113,231	$ 90,231	$ 23,000	$ —

Description	December 31, 2017	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Cash and cash equivalents:				
Cash and money market funds	$ 17,205	$ 17,205	$ —	$ —
Overnight repurchase agreements	15,000	—	15,000	—
Marketable securities:				
U.S. treasury obligations	39,844	39,844	—	—
	$ 72,049	$ 57,049	$ 15,000	$ —

6. Restricted Cash

At September 30, 2018, the Company had $0.9 million in restricted cash of which $0.6 million was classified as short-term and $0.3 million as long-term. At December 31, 2017, the Company had $0.5 million in restricted cash, of which $0.2 million was classified as short-term and $0.3 million as long-term.

As of December 31, 2017, the $0.5 million of restricted cash served as the security deposit on the lease of the Company's current facility in Cambridge, Massachusetts (Note 8). In April 2018, the Company collected a $0.2 million refund from its landlord in accordance with the terms of the lease agreement and the remaining of $0.3 million is classified as long-term on the Company's condensed consolidated balance sheets as of September 30, 2018.

In August 2018, the Company entered into a manufacturing agreement with a third party for manufacturing services related to one of its product candidates. In accordance with the terms of the manufacturing agreement, the Company was required to provide a letter of credit in the amount of $0.6 million. The letter of credit will expire on September 30, 2019 and is classified as short-term on the Company's condensed consolidated balance sheets as of September 30, 2018.

In accordance with the recently adopted accounting pronouncement ASU 2016-18, the following table provides a reconciliation of cash, cash equivalents, and restricted cash reported within the condensed consolidated balance sheets that sum to the total of the amounts shown in the condensed consolidated statement of cash flows as of September 30, 2018, December 31, 2017, September 30, 2017 and December 31, 2016 (in thousands):

	September 30, 2018	December 31, 2017	September 30, 2017	December 31, 2016
Cash and cash equivalents	$ 43,524	$ 32,205	$ 42,149	$ 58,588
Restricted cash, current portion	638	193	193	—
Restricted cash, net of current portion	290	290	290	483
Total cash, cash equivalents and restricted cash	$ 44,452	$ 32,688	$ 42,632	$ 59,071

7. Accrued Expenses

Accrued expenses consisted of the following as of September 30, 2018 and December 31, 2017 (in thousands):

	September 30, 2018	December 31, 2017
External research and preclinical development	$ 7,910	$ 5,875
Employee compensation and benefits	2,461	2,494
Professional fees	695	1,225
Facilities and other	93	134
	$ 11,159	$ 9,728

8. Commitments and Contingencies

Operating Leases

In March 2015, the Company entered into an operating lease for approximately 21,488 rentable square feet of office and laboratory space in Cambridge, Massachusetts (the "2015 Lease"), with a lease term commencing in August 2015 and ending in October 2020. The Company has an option to extend the 2015 Lease for five additional years. The 2015 Lease has escalating rent payments and the Company records rent expense on a straight-line basis over its term, including any rent-free periods. The 2015 Lease includes certain lease incentives in the form of tenant allowances. The Company has capitalized the improvements made with the tenant allowance into fixed assets and established a liability for the deferred lease incentive upon occupancy. The Company recorded these incentives as a component of deferred rent and will amortize these incentives as a reduction of rent expense over the lease term. The related fixed assets will be amortized over the lease term. Upon the Company's adoption of ASC 842 effective January 1, 2019, the lease incentives will be an offsetting component of the right of use asset (see more details in Note 1 – "Recent Accounting Pronouncements" above).

The Company recorded rent expense of $0.2 million for each of the three months ended September 30, 2018 and 2017, and $0.7 million for each of the nine months ended September 30, 2018 and 2017, related to the 2015 Lease. The 2015 Lease required the Company to issue an original letter of credit in the amount of $0.5 million of which $0.2 million was collected in April 2018 and $0.3 million remains classified as restricted cash as of September 30, 2018 (see Note 6).

License Agreements

Dana-Farber Cancer Institute, Inc. and Whitehead Institute for Biomedical Research

In February 2013, the Company entered into a license agreement with Dana-Farber Cancer Institute, Inc. ("Dana-Farber") pursuant to which the Company was granted an exclusive worldwide, sublicensable license under specified patents relating to CDK7 inhibitors and JNK inhibitors owned or controlled by Dana-Farber. Payments totaling $3.4 million are due to Dana-Farber if and when the Company achieves certain clinical and regulatory milestones for any licensed product, none of which have been achieved as of September 30, 2018. No future potential milestone payments have been accrued as September 30, 2018 or December 31, 2017, as no milestones have been achieved and the agreement can be cancelled at the Company's option. Therefore, the Company had no obligation to pay any of these amounts. The Company is obligated to pay a tiered royalty on net sales for licensed products in any country subject to the license. Royalty payments, if any, would continue for the duration of the licensed patents.

In April 2013, the Company entered into a license agreement with the Whitehead Institute for Biomedical Research ("Whitehead") and Dana-Farber, pursuant to which the Company was granted a worldwide, sublicensable license under specified patents relating to MYC modulators owned or controlled by Whitehead and Dana-Farber.

In April 2013, the Company entered into an additional license agreement with Whitehead, pursuant to which the Company was granted a worldwide license under specified patents relating to super-enhancers owned or controlled by Whitehead.

In connection with the Whitehead agreements, the Company issued 171,674 shares of its common stock to Whitehead in April 2013. Payments totaling $3.6 million are due under the Whitehead agreements when the Company achieves certain milestones. The future potential milestone payments due under the Whitehead agreements have not been accrued as of September 30, 2018 or December 31, 2017, as no milestones have been achieved and the agreement can be cancelled at the Company's option. Therefore, the Company had no obligation to pay any of these amounts. The Company paid Whitehead and the Whitehead Institute for Genome Technology Core ("Whitehead Core") $0.5 million and $0.8 million during the nine months ended September 30, 2018 and 2017, respectively, for annual license maintenance fees and research services inclusive of a $0.2 million fee paid to Whitehead as a result of entry into the Collaboration Agreement with Incyte in January 2018. Additionally, at September 30, 2018, the Company had approximately $0.2 million in accounts payable and accrued expenses due to Whitehead for research services performed during 2018.

TMRC Co. Ltd.

In September 2015, the Company entered into an exclusive license agreement with TMRC Co. Ltd. ("TMRC") to develop and commercialize tamibarotene in North America and Europe for the treatment of cancer. This agreement was amended and restated in April 2016.

In exchange for this license, the Company agreed to a non-refundable upfront payment of $1.0 million, for which $0.5 million was paid in September 2015 upon execution of the agreement, and the remaining $0.5 million was paid in May 2016. Under the agreement, the Company is also obligated to make payments upon the successful achievement of clinical and regulatory milestones totaling approximately $13.0 million per indication, defined as a distinct tumor type. In September 2016, the Company paid $1.0 million to TMRC for a development milestone achieved upon the successful dosing of the first patient in its Phase 2 clinical trial of SY-1425. In addition, the Company is obligated to pay TMRC a single-digit percentage royalty, on a country-by-country and product-by-product basis, on net product sales of SY-1425 using know-how and patents licensed from TMRC in North America and Europe for a defined royalty term.

The Company also entered into a supply management agreement with TMRC under which the Company agreed to pay TMRC a fee for each kilogram of SY-1425 active pharmaceutical ingredient that is produced. The Company made payments of $0.4 million under this supply management agreement during the nine months ended September 30, 2017. No payments were made under the supply management agreement during the nine months ended September 30, 2018.

9. Stock-Based Payments

2016 Stock Incentive Plan

The 2016 Stock Incentive Plan (the “2016 Plan”) was adopted by the board of directors on December 15, 2015 and approved by the stockholders on June 17, 2016, and became effective on July 6, 2016 upon the closing of the Company’s initial public offering (“IPO”). The 2016 Plan replaced the 2012 Equity Incentive Plan (the "2012 Plan"). Any options or awards outstanding under the 2012 Plan remained outstanding and effective. Under the 2016 Plan, the Company may grant incentive stock options, non- statutory stock options, stock appreciation rights, restricted stock, restricted stock units and other stock-based awards. The number of shares of the Company’s common stock reserved for issuance under the 2016 Plan automatically increases on the first day of each calendar year, through the 2025 calendar year, in an amount equal to the least of (i) 1,600,000 shares of common stock, (ii) 4.0% of the outstanding shares of common stock as of such date, or (iii) such lesser amount as specified by the board of directors. This number is subject to adjustment in the event of a stock split, stock dividend or other change in the Company’s capitalization. For the calendar year beginning January 1, 2018, the number of shares reserved for issuance under the 2016 Plan was increased by 1,056,935 shares. At September 30, 2018, 2,969,793 shares remained available for future issuance under the 2016 Plan. Under the 2016 Plan, stock options may not be granted at less than fair value on the date of grant.

Terms of stock option agreements, including vesting requirements, are determined by the board of directors, subject to the provisions of the 2016 Plan. Stock option awards granted by the Company generally vest over four years, with 25% vesting on the first anniversary of the vesting commencement date and 75% vesting ratably, on a monthly basis, over the remaining three years. Such awards are exercisable from the date of grant for a period of ten years. The Company may grant performance-based stock option awards for which vesting accelerates upon the achievement of performance-based milestones. For certain of such awards, notwithstanding any vesting in accordance with the achievement of performance-based milestones, such awards may vest in full on the sixth anniversary of the vesting commencement date.

2016 Employee Stock Purchase Plan

The 2016 Employee Stock Purchase Plan (the “2016 ESPP”) was adopted by the board of directors on December 15, 2015 and approved by the stockholders on June 17, 2016, and became effective on July 6, 2016 upon the closing of the IPO. The number of shares of the Company’s common stock reserved for issuance under the 2016 ESPP automatically increases on the first day of each calendar year through the 2025 calendar year, in an amount equal to the least of (i) 1,173,333 shares of the Company’s common stock, (ii) 1.0% of the total number of shares of the Company’s common stock outstanding on the first day of the applicable year, and (iii) an amount determined by the Company’s board of directors. For the calendar year beginning January 1, 2018, the number of shares reserved for issuance under the

2016 ESPP was increased by 264,233 shares. At September 30, 2018, 1,084,756 shares remained available for future issuance under the 2016 ESPP.

Stock Options

Performance-Based Stock Options

The Company has granted stock options to management for which vesting accelerates upon the achievement of performance-based criteria. Milestone events are specific to the Company's corporate goals, including but not limited to certain clinical development milestones and the Company's ability to execute on its corporate development and financing strategies. Stock-based compensation expense associated with these performance-based stock options is recognized based on the accelerated attribution model. Management evaluates when the achievement of a performance-based milestone is probable based on the expected satisfaction of the performance conditions as of the reporting date. Notwithstanding any vesting in accordance with the achievement of performance-based milestones, such awards vest in full on the sixth anniversary of the vesting commencement date. During the nine months ended September 30, 2018, the Company recorded additional stock-based compensation expense of $0.2 million related to the acceleration of vesting of certain stock options associated with the entry into the Collaboration Agreement with Incyte. The Company did not record any additional stock-based compensation expense related to the achievement of performance-based milestones during the three months ended September 30, 2018. As of September 30, 2018, there was $1.1 million of unrecognized stock-based compensation expense related to the performance-based stock options granted to management, with an expected recognition period of 4.01 years.

The Company has granted options to purchase 75,000 shares of common stock to an advisor that vest upon the achievement of performance-based criteria. As of September 30, 2018, no such performance-based criteria had been achieved. As of September 30, 2018, there was $0.7 million of unrecognized compensation cost related to this option, with a remaining contractual period of 7.95 years.

A summary of the status of stock options as of December 31, 2017 and September 30, 2018 and changes during the nine months ended September 30, 2018 is presented below:

	Shares	Weighted Average Exercise Price	Remaining Contractual Life (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2017	2,846,668	$ 9.25	8.2	$ 5,713
Granted	1,358,552	10.90		
Exercised	(103,153)	4.73		
Cancelled	(390,917)	10.95		
Outstanding at September 30, 2018	3,711,150	$ 9.80	8.1	$ 9,358
Exercisable at September 30, 2018	1,354,815	$ 7.50	6.7	$ 6,505

The intrinsic value of stock options exercised during the nine months ended September 30, 2018 and 2017 was $0.8 million and $4.1 million, respectively.

Stock-based Compensation Expense

The fair value of each stock option granted was estimated on the date of grant using the Black-Scholes option-pricing model based on the following weighted-average assumptions:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
Weighted-average risk-free interest rate	2.87 %	2.04 %	2.49 %	2.03 %
Expected dividend yield	- %	- %	- %	- %
Expected option term (in years)	6.08	6.08	6.03	6.01
Volatility	89.71 %	90.84 %	90.34 %	87.22 %

The weighted-average grant date fair value per share of options granted in the nine months ended September 30, 2018 and 2017 was $8.15 and $8.69, respectively.

The following table summarizes the stock-based compensation expense for stock options and restricted common stock granted to employees and non-employees recorded in the Company's condensed consolidated statements of operations:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
Research and development	$ 550	$ 443	$ 1,785	$ 1,221
General and administrative	987	665	3,192	1,927
Total stock-based compensation expense	$ 1,537	$ 1,108	$ 4,977	$ 3,148

As of September 30, 2018, there was $15.5 million of total unrecognized compensation cost related to non-vested stock options granted to employees, excluding those stock option grants subject to the achievement of performance milestones, which is expected to be recognized over a weighted-average period of 3.1 years. Due to an operating loss, the Company does not record tax benefits associated with stock-based compensation or option exercises. Tax benefits will be recorded when realized.

Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our unaudited financial statements and related notes appearing elsewhere in this Quarterly Report on Form 10-Q and the audited financial information and the notes thereto included in our Annual Report on Form 10-K for the year ended December 31, 2017 that we filed with the Securities and Exchange Commission, or SEC, on March 12, 2018, or the 2017 10-K.

Our actual results and timing of certain events may differ materially from the results discussed, projected, anticipated, or indicated in any forward-looking statements. We caution you that forward-looking statements are not guarantees of future performance and that our actual results of operations, financial condition and liquidity, and the development of the industry in which we operate, may differ materially from the forward-looking statements contained in this Quarterly Report. In addition, even if our results of operations, financial condition and liquidity, and the development of the industry in which we operate are consistent with the forward-looking statements contained in this Quarterly Report, they may not be predictive of results or developments in future periods.

The following information and any forward-looking statements should be considered in light of risks identified under the caption "Risk Factors" in the 2017 10-K as updated in Part II, Item 1A of our Quarterly Report on Form 10-Q for the quarter ended March 31, 2018 that we filed with the SEC on May 10, 2018.

We caution readers not to place undue reliance on any forward-looking statements made by us, which speak only as of the date they are made. We disclaim any obligation, except as specifically required by law and the rules of the SEC, to publicly update or revise any such statements to reflect any change in our expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements.

Overview

We are a biopharmaceutical company pioneering an understanding of the non-coding regulatory region of the genome to advance a new wave of medicines that control the expression of genes. We have built a proprietary platform that is designed to systematically and efficiently analyze this unexploited region of DNA in human disease tissue to identify novel targets linked to genomically defined patient populations and to develop drugs against those targets. Because gene expression is fundamental to the function of all cells, we believe that our gene control platform has broad potential to create medicines that achieve profound and durable benefit across therapeutic areas and a range of diseases. We are currently focused on developing treatments for cancer and diseases resulting from modifications of a single gene, also known as monogenic diseases, and are building a pipeline of gene control medicines.

Our lead product candidates are:

- SY-1425, a selective retinoic acid receptor alpha, or RARα, agonist that is being evaluated in combination with azacitidine, a hypomethylating agent frequently used to treat acute myeloid leukemia, or AML, and myelodysplastic syndrome, or MDS, patients, and with daratumumab, an anti-CD38 therapeutic antibody approved to treat multiple myeloma, in a Phase 2 clinical trial in genomically defined subsets of patients with AML and MDS; and

- SY-1365, a selective inhibitor of cyclin-dependent kinase 7, or CDK7, that is in a Phase 1 clinical trial in multiple ovarian and breast cancer patient populations; and

- SY-5609, a novel CDK7 inhibitor that can be administered orally, which is being evaluated in investigational new drug, or IND, enabling preclinical studies.

Our ongoing Phase 2 clinical trial is assessing the safety and efficacy of SY-1425 in combination with azacitidine in approximately 25 newly diagnosed AML patients who are not suitable candidates for standard chemotherapy, and in combination with daratumumab in approximately 12 relapsed or refractory AML and higher-risk MDS patients. Enrollment in the azacitidine combination cohort of the trial began in the fall of 2017 and enrollment in the daratumumab combination cohort of the trial began in early 2018. All patients enrolled or to be enrolled in the trial in support of our primary efficacy analyses have been or will be prospectively selected using our proprietary RARα or IRF8 biomarkers. In addition, to support the development of a commercial companion diagnostic test for SY-1425, we are evaluating SY-1425 in combination with azacitidine in approximately 25 newly diagnosed AML patients who are not suitable candidates for standard chemotherapy and who are biomarker-negative. We expect to report initial clinical data from both combination cohorts of the trial at the American Society of Hematology Annual Meeting in December 2018. To date, we have enrolled 19 patients in the azacitidine combination cohort, including 11 biomarker-positive patients. Eight of these biomarker-positive patients are currently evaluable for clinical responses. To date, we have enrolled 12 patients in the daratumumab combination cohort. Data are currently available on eight of these patients, and six of them are evaluable for clinical responses.

Our Phase 1 clinical trial of SY-1365 is ongoing and we expect to report data from the dose-escalation phase of the trial at the EORTC-NCI-AACR Molecular Targets and Cancer Therapeutics Symposium in November 2018. In September 2018, we opened expansion cohorts in the trial evaluating SY-1365 in multiple ovarian cancer populations as a single agent as well as in combination with carboplatin, a chemotherapeutic agent. The ovarian cancer populations include a 24-patient cohort evaluating SY-1365 as a single agent in patients who have relapsed after three or more prior therapies, a 24-patient cohort evaluating SY-1365 in combination with carboplatin in patients who relapsed after one or more prior therapies but who may still benefit from additional platinum-based treatment, and a 12-patient pilot cohort evaluating SY-1365 as a single agent in primary platinum-refractory disease. We are also evaluating SY-1365 in combination with fulvestrant, a hormonal medicine, in 12 patients with hormone-receptor positive, or HR+, HER2-negative metastatic breast cancer who have progressed after treatment with a CDK4/6 inhibitor plus an aromatase inhibitor. In addition, we are evaluating the mechanism of action of SY-1365 as a single agent in ten patients with any solid tumor accessible for biopsy.

We currently have several other programs in our preclinical and discovery pipeline, including our SY-5609 program, a program directed to inhibitors of an immuno-oncology target, and discovery programs related to a gene control target to treat sickle cell disease and in the field of cancer. We have and are continuing to use our gene control platform in collaboration with third parties to identify and validate targets in diseases beyond our current areas of focus. To this end, we entered into a target discovery, research collaboration and option agreement with Incyte Corporation, or Incyte, in January 2018 under which we are using our platform to identify novel therapeutic targets with a focus on myeloproliferative neoplasms.

Since our inception in November 2011, we have devoted substantially all of our resources to organizing and staffing our company, business planning, raising capital, developing our technology platform and conducting preclinical research and clinical development for our product candidates. We do not have any products approved for sale and have not generated any revenue from product sales. We have financed our operations to date primarily through the sale of equity securities. From inception through September 30, 2018, we raised an aggregate of $288.7 million from such transactions, including $16.6 million in aggregate proceeds through our at-the-market sales facility, $46.0 million in gross proceeds from the sale of common stock in a public offering in February 2018 and $1.4 million in a concurrent private placement

in February 2018, and $10.0 million of aggregate proceeds through the issuance of our common stock in connection with our target discovery collaboration with Incyte in January 2018.

Since inception, we have incurred significant operating losses. Our net losses were $44.2 million and $38.7 million for the nine months ended September 30, 2018 and 2017, respectively. As of September 30, 2018, we had an accumulated deficit of $199.5 million. We expect to continue to incur significant expenses and operating losses for the foreseeable future. We anticipate that our expenses will increase significantly in connection with our ongoing activities, as we:

- continue our planned clinical development activities with respect to SY-1425 and SY-1365 and conduct IND-enabling activities for SY-5609;
- initiate and continue research, preclinical and clinical development efforts for our other gene control programs;
- further develop our gene control platform;
- seek to identify and develop additional product candidates;
- acquire or in-license other product candidates or technologies;
- seek regulatory and marketing approvals for our product candidates that successfully complete clinical trials, if any;
- establish sales, marketing, distribution and other commercial infrastructure in the future to commercialize various products for which we may obtain marketing approval, if any;
- require the manufacture of larger quantities of product candidates for clinical development and, potentially commercialization;
- maintain, expand and protect our intellectual property portfolio;
- hire and retain additional personnel and add operational, financial and management information systems, including personnel and systems to support our product development and commercialization efforts and help us comply with our obligations as a public company; and
- add equipment and physical infrastructure to support our research and development activities.

Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

Financial Operations Overview

Revenue

To date, our revenue has consisted of collaboration and license revenue and we have not generated any revenue from product sales and do not expect to generate any revenue from product sales for the foreseeable future. For the three and nine months ended September 30, 2018, we recognized approximately $0.4 million and $1.2 million of revenue, respectively, all of which was attributable to our target discovery collaboration with Incyte. For the nine months ended September 30, 2017, we recognized $1.1 million of revenue, all of which was attributable to a research agreement with a multinational pharmaceutical company that expired in March 2017 in accordance with its terms. No revenue was recognized during the three months ended September 30, 2017.

Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including development of our gene control platform and the development of product candidates, which include:

- employee-related expenses including salaries and benefits;
- stock-based compensation expense;
- external costs of funding activities performed by third parties that conduct research and development on our behalf and of purchasing supplies used in designing, developing and manufacturing preclinical study and clinical trial materials;
- consulting, licensing and professional fees related to research and development activities; and
- facilities costs, depreciation and amortization and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and other operating costs.

Research and development costs are expensed as incurred. Nonrefundable advance payments made to vendors for goods or services that will be received in the future for use in research and development activities are deferred and capitalized, even when there is no alternative future use for the research and development, until related goods or services are provided.

We typically use our employee, consultant and infrastructure resources across our research and development programs. We track outsourced development costs by product candidate or development program, but we do not allocate personnel costs, other internal costs or certain external consultant costs to specific product candidates or development programs.

The following table summarizes our external research and development expenses by program, as well as expenses not allocated to programs, for the three and nine months ended September 30, 2018 and 2017 (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
SY-1425 external costs	$ 1,723	$ 1,942	$ 5,296	$ 5,945
SY-1365 and other CDK7 program external costs	4,834	2,173	11,956	5,359
Other research and platform programs external costs	1,900	2,335	4,754	6,656
Employee-related expenses, including stock-based compensation	3,331	2,879	10,020	8,823
Facilities and other expenses	1,068	1,118	3,028	3,333
Total research and development expenses	$12,856	$10,447	$35,054	$30,116

We expect our research and development expenses will increase for the foreseeable future as we seek to advance our programs. At this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the development of our product candidates. We are also unable to predict when, if ever, material net cash inflows will commence from sales of our product candidates. This is due to the numerous risks and uncertainties associated with developing such product candidates, including the uncertainty of:

- successful completion of preclinical studies, including activities related to preparation of an IND and minimally efficacious dose studies in animals, where applicable and required, under the requirements of the U.S. Food and Drug Administration, or FDA, or another regulatory authority;
- approval of INDs for our product candidates to commence planned or future clinical trials;

- successful enrollment in, and completion of, clinical trials;
- successful data from our clinical programs that support an acceptable benefit-risk profile of our product candidates in the intended populations;
- successful development, and subsequent clearance or approval, of companion diagnostic tests for use in identifying potential patients;
- receipt of regulatory approvals from applicable regulatory authorities;
- establishment of arrangements with third-party manufacturers for clinical supply and commercial manufacturing and, where applicable, commercial manufacturing capabilities;
- establishment and maintenance of patent and trade secret protection or regulatory exclusivity for our product candidates;
- commercial launch of our product candidates, if and when approved, whether alone or in collaboration with others;
- enforcement and defense of intellectual property rights and claims;
- maintenance of a continued acceptable safety profile of the product candidates following approval; and
- retention of key research and development personnel.

Any changes in the outcome of any of these variables with respect to the development of our product candidates in preclinical and clinical development could mean a significant change in the costs and timing associated with the development of these product candidates. For example, if the FDA or another regulatory authority were to delay our planned start of clinical trials or require us to conduct clinical trials or other testing beyond those that we currently expect or if we experience significant delays in enrollment in any of our planned clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development of our product candidates.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in executive, finance and administrative functions. Other significant costs include corporate facility costs not otherwise included in research and development expenses, legal fees related to patent and corporate matters, and fees for accounting and consulting services.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support our continued research activities and development of our product candidates. We also anticipate that we will incur increased accounting, audit, legal, compliance and director and officer insurance costs, as well as investor and public relations expenses, associated with operating as a public company.

Other Income, Net

Other income, net, consists of interest income on our cash and cash equivalents, interest, dividends, amortization of premiums and discounts and interest expense related to our equipment financing arrangement.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles, or U.S. GAAP. The preparation of these financial statements requires us to make judgments and estimates that affect the reported amounts of assets, liabilities, revenues and expenses and the disclosure of contingent assets and liabilities in our financial statements. We base our estimates on historical experience, known trends and events and various other factors that are believed to be reasonable under the circumstances. Actual results may differ from these estimates under different assumptions or conditions. On an ongoing basis, we evaluate our judgments and estimates in light of changes in

circumstances, facts and experience. The effects of material revisions in estimates, if any, will be reflected in the financial statements prospectively from the date of the change in estimates.

We believe that our most critical accounting policies are those relating to revenue recognition, accrued research and development expenses and stock-based compensation, and there have been no significant changes to our accounting policies discussed in our Annual Report on Form 10-K for the year ended December 31, 2017 that we filed with the SEC on March 12, 2018, other than the adoption of ASU 2014-09 and ASU 2016-18 discussed in the notes to the unaudited condensed consolidated financial statements as of September 30, 2018.

Results of Operations

Comparison of three months ended September 30, 2018 and 2017

The following table summarizes our results of operations for the three months ended September 30, 2018 and 2017, together with the changes in those items in dollars (in thousands):

	Three Months Ended September 30,			
	2018	2017	Dollar Change	% Change
Statements of Operations Data:				
Revenue	$ 412	$ —	$ 412	— %
Operating expenses:				
Research and development	12,856	10,447	2,409	23 %
General and administrative	3,876	3,593	283	8 %
Total operating expenses	16,732	14,040	2,692	19 %
Other income, net	583	215	368	171 %
Net loss	$(15,737)	$(13,825)	$ 1,912	14 %

Revenue

For the three months ended September 30, 2018, we recognized approximately $0.4 million of revenue, all of which is attributable to our target discovery collaboration with Incyte. For the three months ended September 30, 2017, we did not recognize any revenue.

Research and Development Expense

Research and development expense increased by approximately $2.4 million, or 23%, from $10.4 million for the three months ended September 30, 2017 to $12.9 million for the three months ended September 30, 2018. The following table summarizes our research and development expenses for the three months ended September 30, 2018 and 2017, together with the changes to those items in dollars (in thousands):

	Three Months Ended September 30,			
	2018	2017	Dollar Change	% Change
External research and development	$ 7,871	$ 6,017	$ 1,854	31 %
Employee-related expenses, excluding stock-based compensation	2,781	2,436	345	14 %
Stock-based compensation	550	443	107	24 %
Consulting, licensing and professional fees	587	433	154	36 %
Facilities and other expenses	1,067	1,118	(51)	(5)%
Total research and development expenses	$ 12,856	$ 10,447	$ 2,409	23 %

The change in research and development expense was primarily attributable to activities associated with advancing our lead clinical programs, SY-1425 and SY-1365, and preclinical programs as well as enhancing our internal capabilities, including the following:

- an increase of approximately $1.9 million, or 31%, for external research and development costs, primarily due to a $2.4 million increase in contract manufacturing costs associated with our SY-1365 program, offset by a $0.5 million decrease in external preclinical research and development costs;
- an increase of approximately $0.3 million, or 14%, for increased personnel related expenses, including increased salary and benefits, primarily due to our increased headcount;
- an increase of approximately $0.1 million, or 24%, for stock-based compensation expense, also primarily due to our increased headcount; and
- an increase of approximately $0.2 million, or 36%, in consulting, licensing and professional fees primarily due to increased professional fees in support of our SY-1425 and SY-1365 clinical trials.

General and Administrative Expense

General and administrative expense increased by approximately $0.3 million, or 8%, from $3.6 million for the three months ended September 30, 2017 to $3.9 million for the three months ended September 30, 2018. The change in general and administrative expense was primarily attributable to an increase in employee-related costs, including salary, benefits and stock-based compensation.

Other Income, Net

Other income, net, consists of interest income on our cash and cash equivalents, interest and amortization of premiums and discounts on marketable securities, and interest expense related to our equipment financing arrangement. The increase in other income from the three months ended September 30, 2017 to the three months ended September 30, 2018 is due to a higher level of investment in marketable securities.

Comparison of nine months ended September 30, 2018 and 2017

The following table summarizes our results of operations for the nine months ended September 30, 2018 and 2017, together with the changes in those items in dollars (in thousands):

	Nine Months Ended September 30,			
	2018	2017	Dollar Change	% Change
Statements of Operations Data:				
Revenue	$ 1,157	$ 1,101	$ 56	5 %
Operating expenses:				
Research and development	35,054	30,116	4,938	16 %
General and administrative	11,792	10,151	1,641	16 %
Total operating expenses	46,846	40,267	6,579	16 %
Other income, net	1,442	458	984	215 %
Net loss	$(44,247)	$(38,708)	$ 5,539	14 %

Revenue

For the nine months ended September 30, 2018 we recognized approximately $1.2 million of revenue, all of which is attributable to our collaboration agreement with Incyte. For the nine months ended months end September 30, 2017, we recognized $1.1 million of revenue, all of which was attributable to a research agreement with a multinational pharmaceutical company that expired in March 2017 in accordance with its terms.

Research and Development Expense

Research and development expense increased by approximately $5.0 million, or 16%, from $30.1 million for the nine months ended September 30, 2017 to $35.1 million for the nine months ended September 30, 2018. The following table summarizes our research and development expenses for the nine months ended September 30, 2018 and 2017, together with the changes to those items in dollars (in thousands):

	Nine Months Ended September 30,			
	2018	2017	Dollar Change	% Change
External research and development	$20,595	$16,710	$ 3,885	23 %
Employee-related expenses, excluding stock-based compensation	8,235	7,602	633	8 %
Stock-based compensation	1,785	1,221	564	46 %
Consulting, licensing and professional fees	1,410	1,250	160	13 %
Facilities and other expenses	3,029	3,333	(304)	(9)%
Total research and development expenses	$35,054	$30,116	$ 4,938	16 %

The change in research and development expense was primarily attributable to activities associated with advancing our lead clinical and preclinical programs and enhancing our internal capabilities, and included the following:

- an increase of approximately $3.9 million, or 23%, for external research and development costs, including a $4.8 million increase in contract manufacturing costs and a $0.3 million increase in clinical management costs, offset by a $1.3 million decrease in external preclinical research and development costs;
- an increase of approximately $0.6 million, or 8%, for increased personnel related expenses, including increased salary and benefits, primarily due to our increased headcount;
- an increase of approximately $0.6 million, or 46%, for stock-based compensation expense, primarily due to increased headcount as a result of increased operations and the acceleration of vesting of certain performance-based stock options associated with the entry into our target discovery collaboration with Incyte;
- an increase of approximately $0.2 million, or 13%, in consulting, licensing and professional fees primarily due to increased professional fees in support of our SY-1425 and SY-1365 clinical trials; and
- a decrease of approximately $0.3 million, or 9%, in allocable costs for facilities, recruiting and other costs that were incurred in the nine months ended September 30, 2017, that did not reoccur during the nine months ended September 30, 2018.

General and Administrative Expense

General and administrative expense increased by approximately $1.6 million, or 16%, from $10.2 million for the nine months ended September 30, 2017 to $11.8 million for the nine months ended September 30, 2018. The change in general and administrative expense was primarily attributable to an increase in employee-related costs, including salary, benefits and stock-based compensation, primarily due to our increased headcount period over period and the acceleration of certain performance-based stock options associated with entry into our target discovery collaboration with Incyte in January 2018.

Other Income, Net

Other income, net consists of interest income on our cash and cash equivalents, interest and amortization of premiums and discounts on marketable securities, and interest expense related to our equipment financing arrangement. The increase in other income from the nine months ended September 30, 2017, to the nine months ended September 30, 2018 is due to a higher level of invested cash, cash equivalents and marketable securities arising out of

the proceeds of our February 2018 underwritten public offering and concurrent private placement, entry into our target discovery collaboration with Incyte, and proceeds received from the use of our at-the-market sales facility.

Liquidity and Capital Resources

Sources of Liquidity

We funded our operations from inception through September 30, 2018, primarily through the sale of equity securities and research agreements with third parties, including our collaboration with Incyte.

On July 20, 2017, we filed a universal shelf registration statement on Form S-3 with the SEC to register for sale from time to time up to $225.0 million of common stock, preferred stock, debt securities, warrants and/or units in one or more registered offerings. The shelf registration statement was declared effective on July 31, 2017. Further, in July 2017, we entered into an at-the-market sales agreement with Cowen & Co., or Cowen, pursuant to which we may offer and sell shares of our common stock having an aggregate offering price of up to $50.0 million through Cowen pursuant to such universal shelf registration statement. As of September 30, 2018, we had $33.4 million remaining for issuance under the sales agreement.

In February 2018, we raised aggregate gross proceeds of $46.0 million in a public offering effected through our shelf registration statement, before deducting underwriting discounts and commissions.

As of September 30, 2018, $162.4 million of securities remained available for issuance under the shelf registration agreement.

As of September 30, 2018, we had cash, cash equivalents and marketable securities of approximately $113.2 million.

Cash Flows

The following table provides information regarding our cash flows for the nine months ended September 30, 2018 and 2017 (in thousands):

	Nine Months Ended September 30,	
	2018	2017
Net cash (used in) provided by:		
Operating activities	$(26,503)	$(34,162)
Investing activities	(30,680)	(15,522)
Financing activities	68,947	33,245
Net increase (decrease) in cash, cash equivalents and restricted cash	$ 11,764	$(16,439)

Net Cash Used in Operating Activities

The use of cash in both periods resulted primarily from our net losses adjusted for non-cash charges and changes in components of working capital.

Net cash used in operating activities was $26.5 million during the nine months ended September 30, 2018 compared to $34.2 million for the nine months ended September 30, 2017. The decrease in cash used in operating activities was primarily due to proceeds received upon entry into the Incyte target discovery collaboration during the nine months ended September 30, 2018.

Net Cash Used in Investing Activities

Net cash used in investing activities was $30.7 million during the nine months ended September 30, 2018 compared to $15.5 million during the nine months ended September 30, 2017. The increase in cash used in investing activities was primarily due to the net purchases of marketable securities of $29.5 million during the nine months ended September 30,

2018 as compared net purchases of marketable securities of $14.8 million during the nine months ended September 30, 2017.

Net Cash Provided by Financing Activities

Net cash provided by financing activities was $68.9 million during the nine months ended September 30, 2018 compared to $33.2 million for the nine months ended September 30, 2017. Cash provided by financing activities for the nine months ended September 30, 2018 was primarily due to net proceeds of $42.8 million from the sale of our common stock in an underwritten public offering in February 2018, $1.4 million in proceeds from our February 2018 private placement, $7.7 million in proceeds attributable to the equity investment made by Incyte in connection with entry into our target discovery collaboration, $16.6 million in proceeds through the use of our at-the-market sales facility, and $0.5 million from the exercise of employee stock options, offset by payments under our capital lease obligations. Net cash provided by financing activities for the nine months ended September 30, 2017 was primarily attributable to the private placement of our common stock for gross proceeds of $35.0 million in April 2017, resulting in net proceeds of $32.6 million and $0.9 million from the exercise of employee stock options.

Funding Requirements

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue clinical trials of SY-1425 and SY-1365, advance additional product candidates such as SY-5609 through preclinical development and into clinical trials, seek to develop companion diagnostic tests for use with our product candidates, initiate new research and preclinical development projects and seek marketing approval for any product candidates that we successfully develop. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to establishing sales, marketing, distribution and other commercial infrastructure to commercialize such products. Furthermore, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on favorable terms, we would be forced to delay, reduce, eliminate, or out-license our research and development programs or future commercialization rights to our product candidates.

We believe that our cash, cash equivalents and marketable securities as of September 30, 2018 will enable us to fund our planned operating expense and capital expenditure requirements into 2020. Our future capital requirements will depend on many factors, including:

- the scope, progress, timing, costs and results of clinical trials of SY-1425 and SY-1365 and any associated companion diagnostic tests, as well as the scope, progress, timing, costs and results of IND-enabling studies of SY-5609;
- research and preclinical development efforts for any future product candidates that we may develop;
- the number of future product candidates that we pursue and their development requirements;
- our ability to enter into and the terms and timing of any collaborations, licensing agreements or other arrangements;
- whether our target discovery collaboration with Incyte will yield any validated targets, whether Incyte will exercise any of its options to exclusively license intellectual property directed to such targets, and whether and when any of the target validation fees, option exercise fees, milestone payments or royalties under the collaboration agreement with Incyte will ever be paid;
- the outcome, timing and costs of seeking regulatory approvals;
- the costs of commercialization activities for any of our product candidates that receive marketing approval to the extent such costs are not the responsibility of any future collaborators, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- the costs of acquiring potential new product candidates or technology;

- the costs of any physician education programs relating to selecting and treating genomically defined patient populations;
- the timing and amount of milestone and other payments due to licensors for patent and technology rights used in our development platform;
- revenue received from commercial sales, if any, of our current and future product candidates;
- our headcount growth and associated costs as we expand our research and development, operate as a public company, and establish a commercial infrastructure;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against intellectual property related claims; and
- the costs of operating as a public company.

Identifying potential product candidates and conducting preclinical studies and clinical trials is a time-consuming, expensive and uncertain process that takes many years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our common stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise funds through additional collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations and Commitments

During the nine months ended September 30, 2018, there were no material changes to our contractual obligations and commitments described under the caption “Management’s Discussion and Analysis of Financial Condition and Results of Operations” in our Annual Report on Form 10-K for the year ended December 31, 2017 that we filed with the SEC on March 12, 2018.

Off-Balance Sheet Arrangements

We did not have, during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under applicable SEC rules.

Item 3. Quantitative and Qualitative Disclosures About Market Risk

We are exposed to market risk related to changes in interest rates. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments, including cash equivalents, are in the form of money market funds and marketable securities and are invested in U.S. treasury or government obligations. However, because of the short-term nature of the duration of our portfolio and the low-risk profile of our investments, we believe an immediate 10% change in market interest rates

would not be expected to have a material impact on the fair market value of our investments portfolio or on our financial condition or results of operations.

We are also exposed to market risk related to changes in foreign currency exchange rates. We contract with vendors that are located in Asia and Europe and certain invoices are denominated in foreign currencies. We are subject to fluctuations in foreign currency rates in connection with these arrangements. We do not currently hedge our foreign currency exchange rate risk. As of September 30, 2018, we had no liabilities denominated in foreign currencies.

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation had a material effect on our business, financial condition or results of operations during the nine months ended September 30, 2018 and 2017.

Item 4. Controls and Procedures

Management's Evaluation of our Disclosure Controls and Procedures

We maintain "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms and (2) accumulated and communicated to our management, including our principal executive and principal financial officer, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our disclosure controls and procedures are designed to provide reasonable assurance of achieving their control objectives.

Our management, with the participation of our Chief Executive Officer, who serves as our Principal Executive Officer, and our Chief Financial Officer, who serves as our Principal Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures as of September 30, 2018, the end of the period covered by this Quarterly Report on Form 10-Q. Based upon such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of such date.

Changes in Internal Control over Financial Reporting

Effective January 1, 2018, we adopted the provisions of ASC 606, *Revenue from Contracts with Customers*. As part of the adoption of this standard, we reviewed our control procedures and have modified certain of our processes to ensure compliance with the new standard.

Other than the foregoing, during the nine months ended September 30, 2018, there were no changes in our internal control over financial reporting that occurred during the period covered by this Quarterly Report on Form 10-Q that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II – OTHER INFORMATION

Item 1A. Risk Factors.

The following information updates, and should be read in conjunction with, the risk factors discussed in Part I, Item 1A, "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2017, as amended in Part II, Item 1A, "Risk Factors" in our Quarterly Reports on Form 10-Q for the quarters ended March 31 and June 30, 2018. Any of the risk factors contained in this Quarterly Report on Form 10-Q and those reports could materially affect our business, financial condition or future results, and such risk factors may not be the only risks we face. Additional risks and uncertainties not currently known to us or that we currently deem to be immaterial also may materially adversely affect our business, financial condition or future results.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses since inception, expect to incur significant and increasing losses for at least the next several years, and may never achieve or maintain profitability.

We have incurred significant annual net operating losses in every year since our inception. We expect to continue to incur significant and increasing net operating losses for at least the next several years. Our net losses were $29.8 million, $47.7 million and $54.0 million for the years ended December 31, 2015, 2016 and 2017, respectively, and were $44.2 million for the nine months ended September 30, 2018. As of September 30, 2018, we had an accumulated deficit of $199.5 million. We have not generated any revenues from product sales, have not completed the development of any product candidate and may never have a product candidate approved for commercialization. We have financed our operations to date primarily through the sale of equity securities. We have devoted substantially all of our financial resources and efforts to research and development and general and administrative expense to support such research and development. Our net losses may fluctuate significantly from quarter to quarter and year to year. Net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity (deficit) and working capital.

We anticipate that our expenses will increase substantially if and as we:

- continue our planned clinical development activities with respect to SY-1425, a selective retinoic acid receptor alpha, or RARα, agonist that is currently being evaluated in combination with azacitidine, a hypomethylating agent, and with daratumumab, an anti-CD38 antibody, in a Phase 2 clinical trial, SY-1365, a selective inhibitor of cyclin-dependent kinase 7, or CDK7, that is currently being evaluated as a single agent and in combination in a Phase 1 clinical trial in multiple ovarian and breast cancer populations, and SY-5609, an oral CDK7 inhibitor that is entering investigational new drug, or IND, enabling studies;
- develop and seek approval of companion diagnostic tests for use in identifying patients who may benefit from treatment with our products and product candidates;
- initiate and continue research, preclinical and clinical development efforts for our current research and preclinical programs;
- further develop our gene control platform;
- seek to identify and develop additional product candidates;
- acquire or in-license other product candidates or technologies;
- seek regulatory and marketing approvals for our product candidates that successfully complete clinical trials, if any;
- establish sales, marketing, distribution and other commercial infrastructure in the future to commercialize various products for which we may obtain marketing approval, if any;
- require the manufacture of larger quantities of product candidates for clinical development and, potentially, commercialization;
- maintain, expand and protect our intellectual property portfolio;
- hire and retain additional personnel and add operational, financial and management information systems, including personnel and systems to support our product development and commercialization efforts and help us comply with our obligations as a public company; and
- add equipment and physical infrastructure to support our research and development programs.

Our ability to become and remain profitable depends on our ability to generate revenue. We do not expect to generate significant revenue unless and until we are, or any future collaborator is, able to obtain marketing approval for, and successfully commercialize, one or more of our product candidates. Successful commercialization will require achievement of key milestones, including initiating and successfully completing clinical trials of our product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those products for which we, or any of our future collaborators, may obtain marketing approval, satisfying any post-marketing requirements and obtaining reimbursement for our products from private insurance or government payors. Because of the uncertainties and risks associated with these activities, we are unable to accurately predict the timing and amount of revenues, and if or when we might achieve profitability. We and any future collaborators may never succeed in these activities and, even if we do, or any future collaborators do, we may never generate revenues that are large enough for us to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our pipeline of product candidates or continue our operations and cause a decline in the value of our common stock.

We will need substantial additional funding, and if we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a very time consuming, expensive and uncertain process that takes years to complete. We expect our expenses to increase in connection with our ongoing activities, particularly with respect to our ongoing Phase 2 clinical trial of SY-1425 in combination with azacitidine and daratumumab and the development of a companion diagnostic test for use in identifying patients who may benefit from treatment with SY-1425, advance the ongoing clinical development of SY-1365 through Phase 1 expansion cohorts in ovarian and breast cancers, advance SY-5609 through IND-enabling studies, initiate new research, preclinical and clinical development efforts, and seek marketing approval for any product candidates and companion diagnostic tests that we or a vendor successfully develop. Moreover, under license agreements with various licensors, we are obligated to make milestone payments upon the successful completion of specified development and commercialization activities for products or product candidates covered by licensed intellectual property rights. In addition, if we obtain marketing approval for any product candidate that we may successfully develop, we may incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of a future collaborator. Furthermore, we expect to incur significant costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we may be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

We will be required to expend significant funds in order to advance the development of SY-1425, SY-1365 and SY-5609, as well as our other research and preclinical programs. In addition, while we may seek one or more collaborators for future development of our current product candidates or any future product candidates that we may develop for one or more indications, we may not be able to enter into a collaboration for any of our product candidates for such indications on suitable terms, on a timely basis, or at all. In any event, our existing cash, cash equivalents and marketable securities will not be sufficient to fund all of the efforts that we plan to undertake or to fund the completion of development of our product candidates or our other preclinical programs. Accordingly, we will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources. We do not have any committed external source of funds to support our internal research and development efforts. Adequate additional financing may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy.

We believe that our existing cash, cash equivalents and marketable securities as of September 30, 2018 will enable us to fund our planned operating expense and capital expenditure requirements into 2020. Our estimate as to how long we expect our existing cash, cash equivalents, and marketable securities to be able to continue to fund our operations is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Further, changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned. Our future funding requirements, both short-term and long-term, will depend on many factors, including:

- the scope, progress, timing, costs and results of clinical trials of SY-1425 and SY-1365 and any associated companion diagnostic tests as well as the scope, progress, timing, costs and results of IND-enabling studies of SY-5609;
- research and preclinical development efforts for any future product candidates that we may develop;
- the number of future product candidates that we pursue and their development requirements;
- our ability to enter into, and the terms and timing of, any collaborations, licensing agreements or other arrangements;
- whether our target discovery collaboration with Incyte Corporation, or Incyte, will yield any validated targets, whether Incyte will exercise any of its options to exclusively license intellectual property directed to such targets, and whether and when any of the target validation fees, option exercise fees, milestone payments or royalties under the collaboration agreement with Incyte will ever be paid;
- the outcome, timing and costs of seeking regulatory approvals;
- the costs of commercialization activities for any of our product candidates that receive marketing approval to the extent such costs are not the responsibility of any future collaborators, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- the costs of acquiring potential new product candidates or technology;
- the costs of any physician education programs relating to selecting and treating genomically defined patient populations;
- the timing and amount of milestone and other payments due to licensors for patent and technology rights used in our development platform;
- revenue received from commercial sales, if any, of our current and future product candidates;
- our headcount growth and associated costs as we expand our research and development, operate as a public company, and establish a commercial infrastructure;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against intellectual property related claims; and
- the costs of operating as a public company.

Risks Related to the Discovery, Development and Commercialization of Product Candidates

If clinical trials of any product candidates that we, or any future collaborators, may develop fail to satisfactorily demonstrate safety and efficacy to the FDA and other regulators, we, or any future collaborators, may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of these product candidates.

We, and any future collaborators, are not permitted to commercialize, market, promote or sell any product candidate in the United States without obtaining marketing approval from the U.S. Food and Drug Administration, or FDA. Foreign regulatory authorities, such as the European Medicines Agency, or the EMA, impose similar requirements. We, and any future collaborators, must complete extensive preclinical development and clinical trials to demonstrate the safety and efficacy of our product candidates in humans before we will be able to obtain these approvals.

We are conducting a Phase 2 clinical trial of SY-1425 in combination with azacitidine in genomically defined subsets of patients with newly-diagnosed acute myeloid leukemia, or AML, who are not suitable candidates for standard chemotherapy, and in combination with daratumumab in genomically defined patients with relapsed or refractory AML or higher-risk myelodysplastic syndrome, or MDS, identified using our RARα and IRF8 biomarkers. We anticipate reporting initial clinical data from this trial at the American Society of Hematology Annual Meeting to be held in December 2018. In addition, to support the development of a commercial companion diagnostic test for SY-1425, we are also enrolling in the trial newly diagnosed AML patients who are not suitable candidates for standard chemotherapy and who are biomarker-negative to further evaluate SY-1425 in combination with azacitidine. Our anticipated time to data in this trial and the quantity of data to be presented from this trial is and will continue to be subject to our continued ability to initiate clinical trial sites and recruit eligible patients, the performance of the clinical trial assay being used in the trial and the prevalence of patients with these biomarkers, and the satisfaction by biomarker-positive patients of other eligibility criteria for participation in the trial. The rate of patient enrollment in the trial is difficult to predict. As a result, there can be no assurance that we will enroll or have data from the trial when we anticipate.

We are also conducting a Phase 1 clinical trial of SY-1365 in patients with advanced solid tumors. We have expanded this trial in multiple ovarian and breast cancer populations and plan to report initial clinical data from the dose- escalation portion of this trial at the EORTC-NCI-AACR Molecular Targets and Cancer Therapeutics Symposium to be held in November 2018. Our assumptions as to the activity of SY-1365 at particular dose levels may prove to be incorrect. There can be no assurance that we will enroll or have data from the trial when we anticipate.

Clinical testing is expensive, is difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. The clinical development of our product candidates is susceptible to the risk of failure inherent at any stage of product development, including failure to demonstrate efficacy in a clinical trial or across a broad population of patients, the occurrence of adverse events that are severe or medically or commercially unacceptable, failure to comply with protocols or applicable regulatory requirements and determination by the FDA or any comparable foreign regulatory authority that a product candidate may not continue development or is not approvable. It is also possible that, even if one or more of our product candidates has a beneficial effect, that effect will not be detected during clinical evaluation as a result of one or more of a variety of factors, including the size, duration, design, measurements, conduct or analysis of our clinical trials. For example, in December 2017 we reported data from our Phase 2 clinical trial evaluating SY-1425 as a single agent in genomically defined subsets of patients with relapsed or refractory AML and higher-risk MDS. While biological and clinical activity was observed in certain patients enrolled in the trial, the data were not sufficiently robust to warrant further development of SY-1425 as a single agent in these patient populations and we elected to cease further development in the portions of our Phase 2 clinical trial evaluating SY-1425 as a single agent. We face a similar risk of failure in our ongoing evaluation of SY-1425 in combination with azacitidine and daratumumab. Conversely, as a result of the same factors, our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any. Similarly, in our clinical trials we may fail to detect toxicity of or intolerability caused by our product candidates, or mistakenly believe that our product candidates are toxic or not well tolerated when that is not in fact the case.

Any inability to successfully complete preclinical and clinical development could result in additional costs to us, or any future collaborators, and impair our ability to generate revenues from product sales, regulatory and commercialization milestones and royalties. Moreover, if we, or any future collaborators, are required to conduct additional clinical trials or other testing of our product candidates beyond the trials and testing that we or they contemplate, if we, or they, are unable to successfully complete clinical trials of our product candidates or other testing, or the results of these trials or tests are unfavorable, uncertain or are only modestly favorable, or there are unacceptable safety concerns associated with our product candidates, we, or any future collaborators, may:

- incur additional unplanned costs;
- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;

- obtain approval with labeling that includes significant use or distribution restrictions or significant safety warnings, including boxed warnings;
- be subject to additional post-marketing testing or other requirements; or
- be required to remove the product from the market after obtaining marketing approval.

Our failure to successfully initiate and complete clinical trials of our product candidates and to demonstrate the efficacy and safety necessary to obtain regulatory approval to market any of our product candidates would significantly harm our business.

Adverse events or undesirable side effects caused by, or other unexpected properties of, product candidates that we develop may be identified during development and could delay or prevent their marketing approval or limit their use.

Adverse events or undesirable side effects caused by, or other unexpected properties of, SY-1425, SY-1365 or any future product candidates that we may develop could cause us, any future collaborators, an institutional review board or regulatory authorities to interrupt, delay or halt clinical trials of one or more of our product candidates and could result in a more restrictive label or the delay or denial of marketing approval by the FDA or comparable foreign regulatory authorities. Because gene control techniques are relatively new, side effects from gene control approaches may be unpredictable. Tamibarotene, the active ingredient in SY-1425, has been observed to be associated with adverse events, such as mild or moderate dry skin, skin rash, headache and bone pain, as well as retinoic acid syndrome and elevated levels of cholesterol, lipids, liver function enzymes and white blood cells, which were severe in certain cases. Furthermore, retinoids such as SY-1425 may cause birth defects and therefore may carry a warning on their label. Other examples of retinoids, a class of chemical compounds that are related to vitamin A, include all trans retinoic acid (also known as ATRA), Retin-A, retinol (found in over-the-counter skin creams), isotretinoin and bexarotene. In addition, our experience administering SY-1365 to humans has been limited to date, so the safety profile that SY-1365 will demonstrate in human clinical trials remains uncertain. We are evaluating the administration of tamibarotene in combination with azacitidine and daratumumab, in patients with AML and MDS. We are also evaluating SY-1365 in combination with carboplatin in patients with ovarian cancer and fulvestrant in patients with metastatic breast cancer. We cannot predict at this time whether the combination of our product candidates with another product, or with any premedication administered to mitigate potential side effects, will be well tolerated by patients in clinical studies or that any unexpected adverse events or undesirable side effects will not occur. If any of our product candidates is associated with adverse events or undesirable side effects or has properties that are unexpected, we, or any future collaborators, may need to abandon development or limit development of that product candidate to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that initially showed promise in clinical or earlier stage testing have later been found to cause undesirable or unexpected side effects that prevented further development of the compound.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The development and commercialization of new products is highly competitive. We expect that we, and any future collaborators, will face significant competition from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide with respect to any of our product candidates that we, or any future collaborators, may seek to develop or commercialize in the future. Specifically, there are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of product candidates for the treatment of the key indications of our most advanced programs. For example, we are aware of five new drugs approved by the FDA since 2017 for the treatment of AML or patient subsets within AML: midostaurin, enasidanib, ivosidenib, daunorubicin + cytarabine liposome, and gemtuzumab ozogamicin. SY-1425 may also face competition from other investigational products currently in clinical development for AML and MDS, including venetoclax, for which marketing approval is currently being sought by AbbVie, Inc. for the treatment of patients with AML, as well as investigational products in development from Takeda Pharmaceutical Co. Ltd., Daiichi Sankyo Company, Limited, Agios Pharmaceuticals, Inc., Novartis AG, Bristol-Myers Squibb Co., Eli Lilly & Co., Eisai Inc., Celgene Corporation, Pfizer, Inc., Incyte Corporation and FORMA Therapeutics, LLC. We are aware of only one other selective RARα program, a compound in development from Io Therapeutics, Inc. which, according to a government-sponsored website, is in an investigator-initiated Phase 1/2 study in a non-selective patient group in relapsed

and refractory AML, high-risk MDS and chronic myelomonocytic leukemia. In addition, we are aware of an oral CDK7 inhibitor being developed by Carrick Therapeutics Ltd. that is currently being evaluated in a Phase 1 clinical trial and several other selective CDK7 inhibitor programs that we believe are in preclinical development, including programs from Aurigene Discovery Technologies Ltd., Ube Industries Ltd., Qurient Co. Ltd., and Beta Pharma, Inc. SY-1365 may face competition from these selective CDK7 inhibitors. There is also significant competition in the field of ovarian cancer. For example, AstraZeneca plc has recently reported positive data on its PARP inhibitor, olaparib, in this disease, and we are aware of late-stage clinical programs in ovarian cancer being conducted by such companies as Pfizer, Inc., ImmunoGen, Inc., Tesaro, Inc. and Merck Sharp & Dohme Corp. HR+ breast cancer is also a competitive field, with indication expansion activities being conducted by Pfizer, Inc., Novartis AG and Eli Lilly & Co. for their respective CDK4/6 inhibitors, and with PI3K inhibitors such as alpelisib.

Our competitors may succeed in developing, acquiring or licensing technologies and products that are more effective, have fewer side effects or more tolerable side effects or are less costly than any product candidates that we are currently developing or that we may develop, which could render our product candidates obsolete and noncompetitive.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer or more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we, or any future collaborators, may develop. For example, the evolving standard of care for the treatment of patients with AML and the response rates and duration of response seen with approved and investigational agents in this disease may result in a longer and more complex clinical development path for SY-1425, which in turn will impact the potential return on investments in clinical trials of SY-1425. Our competitors also may obtain FDA or other marketing approval for their products before we, or any future collaborators, are able to obtain approval for ours, which could result in our competitors establishing a strong market position before we, or any future collaborators, are able to enter the market.

Many of our existing and potential future competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining marketing approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, the development of our product candidates.

Risks Related to Regulatory Approval and Marketing of Our Product Candidates and Other Legal Compliance Matters

We, or any future collaborators, may not be able to obtain orphan drug designation or orphan drug exclusivity for our product candidates and, even if we do, that exclusivity may not prevent the FDA or the EMA from approving competing products.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States. We have obtained orphan drug designation for SY-1425 for the treatment of AML in the United States and in Europe. In the future, however, we or any future collaborators may seek orphan drug designations for SY-1425 in other indications or territories or for other product candidates and may be unable to obtain such designations.

Even if we, or any future collaborators, obtain orphan drug designation for a product candidate, we, or they, may not be able to obtain orphan drug exclusivity for that product candidate. Generally, a product with orphan drug designation only becomes entitled to orphan drug exclusivity if it receives the first marketing approval for the indication for which it has such designation, in which case the FDA or the EMA will be precluded from approving another marketing application for the same drug for that indication for the applicable exclusivity period. The applicable exclusivity period is seven years in the United States and ten years in Europe. The European exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or the EMA determines that the

request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

Even if we, or any future collaborators, obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition and the same drug can be approved for different conditions. Even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

On August 3, 2017, Congress passed the FDA Reauthorization Act of 2017 which, among other things, codified the FDA's pre-existing regulatory interpretation, to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

Item 6. Exhibits.

Exhibit No.	Description of Exhibit
3.1	Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-37813) filed on July 6, 2016).
3.2	Amended and Restated By-Laws of the Registrant (incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K (File No. 001-37813) filed on July 6, 2016).
31.1	Certification of principal executive officer pursuant to Rule 13a-14(a) promulgated under the Securities Exchange Act of 1934, as amended.
31.2	Certification of principal financial officer pursuant to Rule 13a-14(a) promulgated under the Securities Exchange Act of 1934, as amended.
32.1	Certification of principal executive officer pursuant to Rule 13a-14(b) promulgated under the Securities Exchange Act of 1934, as amended, and Section 1350 of Chapter 63 of Title 18 of the United States Code.
32.2	Certification of principal financial officer pursuant to Rule 13a-14(b) promulgated under the Securities Exchange Act of 1934, as amended, and Section 1350 of Chapter 63 of Title 18 of the United States Code.
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Label Linkbase Document
101.PRE	XBRL Taxonomy Presentation Linkbase Document

SIGNATURES

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 thereunto duly authorized.

Syros Pharmaceuticals, Inc.

Date: November 1, 2018

By: /s/ Joseph J. Ferra Jr.
Joseph J. Ferra Jr.
Chief Financial Officer (Principal Financial Officer)

Exhibit 31.1

Certification of Principal Executive Officer pursuant to Exchange Act Rules 13a-14(a) and 15d-14(a), as adopted pursuant to Section 302 of Sarbanes-Oxley Act of 2002

I, Nancy Simonian, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Syros Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report), that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Syros Pharmaceuticals, Inc.

/s/ Nancy Simonian, M.D.
Nancy Simonian, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

Dated: November 1, 2018

Exhibit 31.2

Certification of Principal Financial Officer pursuant to Exchange Act Rules 13a-14(a) and 15d-14(a), as adopted pursuant to Section 302 of Sarbanes-Oxley Act of 2002

I, Joseph J. Ferra, Jr., certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Syros Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report), that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Syros Pharmaceuticals, Inc.

/s/ Joseph J. Ferra, Jr.
Joseph J. Ferra, Jr.
Chief Financial Officer
(Principal Financial Officer)

Dated: November 1, 2018

Exhibit 32.1

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Quarterly Report on Form 10-Q of Syros Pharmaceuticals, Inc. (the "Company") for the quarter ended September 30, 2018 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Nancy Simonian, President and Chief Executive Officer of the Company, hereby certifies, pursuant to Section 1350 of Chapter 63 of Title 18, United States Code, that to her knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: November 1, 2018

/s/ Nancy Simonian, M.D.
Nancy Simonian, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.

Exhibit 32.2

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Quarterly Report on Form 10-Q of Syros Pharmaceuticals, Inc. (the "Company") for the quarter ended September 30, 2018 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Joseph J. Ferra Jr., Chief Financial Officer of the Company, hereby certifies, pursuant to Section 1350 of Chapter 63 of Title 18, United States Code, that to his knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: November 1, 2018

/s/ Joseph J. Ferra, Jr.
Joseph J. Ferra, Jr.
Chief Financial Officer
(Principal Financial Officer)

A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.