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 March 31, 2021

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.)**
35 CambridgePark Drive, 4th Floor **Cambridge, Massachusetts** **(Address of Principal Executive Offices)**	**02140** **(Zip Code)**

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

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	Trading Symbol(s)	Name of Each Exchange on Which Registered
Common Stock, $0.001 par value	**SYRS**	**Nasdaq Global Select Market**

Indicate by check mark whether the registrant (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.

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 April 30, 2021: 61,858,267

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Cautionary Note Regarding Forward-Looking Statements and Industry Data

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:

- our plans to initiate and expand clinical trials of our product candidates and our expectations for the timing, quantity and quality of information to be reported from our clinical trials of SY-1425, SY-2101 and SY-5609;
- 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 ability to discover and develop compounds suitable for clinical development and the timing for designation of future development candidates;
- our ability to replicate in any clinical trial of one of our product candidates the results we observed in preclinical or earlier clinical studies of such product candidate;
- our plans to research, develop, seek approval for, 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 a drug candidate will be nominated to enter investigational new drug application-enabling studies under our sickle cell disease collaboration with Global Blood Therapeutics, Inc., or GBT, whether GBT will exercise its option to exclusively license intellectual property arising from the collaboration, whether and when any option exercise fees, milestone payments or royalties under the collaboration agreement with GBT will ever be paid, and whether we exercise our U.S. co-promotion option under the GBT agreement;
- 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 Incyte collaboration will ever be paid;
- the potential benefits of any future collaboration;
- developments relating to our competitors and our industry;
- the impact of government laws and regulations;

- the timing of and our ability to file new drug applications and 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 and cash equivalents 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. In particular, the extent to which the COVID-19 outbreak continues to impact our operations and those of the third parties on which we rely will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the duration and severity of the outbreak, additional or modified government actions, and the actions that may be required to contain the virus or treat its impact. COVID-19 has and may continue to adversely impact our operations and workforce, including our discovery research, supply chain and clinical trial operations activities, which in turn could have an adverse impact on our business and financial results.

Our forward-looking statements also do not reflect the potential impact of any future acquisitions, mergers, dispositions, collaborations, joint ventures or investments that we may make or enter into.

This report also includes statistical and other industry and market data that we obtained from industry publications and research, surveys, and studies conducted by third parties as well as our own estimates. All of the market data used in this report involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. Industry publications and third-party research, surveys, and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our estimates of the potential market opportunities for our drug candidates include several key assumptions based on our industry knowledge, industry publications, third-party research, and other surveys, which may be based on a small sample size and may fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions.

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)

	March 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 222,142	$ 173,984
Accounts receivable	—	7
Contract assets	2,622	2,324
Prepaid expenses and other current assets	1,913	2,242
Total current assets	226,677	178,557
Property and equipment, net	13,927	14,213
Other long-term assets	1,743	1,966
Restricted cash	3,086	3,086
Right-of-use asset – operating lease	14,662	14,831
Right-of-use assets – financing leases	532	597
Total assets	$ 260,627	$ 213,250
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 3,660	$ 3,603
Accrued expenses	9,127	11,084
Deferred revenue, current portion	12,786	12,209
Financing lease obligations, current portion	271	265
Operating lease obligation, current portion	1,525	1,463
Total current liabilities	27,369	28,624
Deferred revenue, net of current portion	7,166	9,877
Financing lease obligations, net of current portion	286	356
Operating lease obligation, net of current portion	24,167	24,578
Warrant liability	12,041	19,711
Debt, net of debt discount, long term	39,718	39,551
Commitments and contingencies (See Note 9)		
Stockholders' equity:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized at March 31, 2021 and December 31, 2020; 0 shares issued and outstanding at March 31, 2021 and December 31, 2020	—	—
Common stock, $0.001 par value; 200,000,000 shares authorized at March 31, 2021 and December 31, 2020; 61,849,642 and 56,222,746 shares issued and outstanding at March 31, 2021 and December 31, 2020, respectively	61	56
Additional paid-in capital	541,068	467,518
Accumulated deficit	(391,249)	(377,021)
Total stockholders' equity	149,880	90,553
Total liabilities and stockholders' equity	$ 260,627	$ 213,250

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 March 31,	
	2021	**2020**
Revenue	$ 4,827	$ 2,379
Operating expenses:		
Research and development	20,029	14,569
General and administrative	5,739	5,149
Total operating expenses	25,768	19,718
Loss from operations	(20,941)	(17,339)
Interest income	10	384
Interest expense	(967)	(271)
Change in fair value of warrant liability	7,670	—
Net loss applicable to common stockholders	$ (14,228)	$ (17,226)
Net loss per share applicable to common stockholders - basic and diluted	$ (0.23)	$ (0.39)
Weighted-average number of common shares used in net loss per share applicable to common stockholders - basic and diluted	61,379,641	43,923,999

See accompanying notes to unaudited condensed consolidated financial statements.

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

	Three Months Ended March 31,	
	2021	2020
Net loss	$ (14,228)	$ (17,226)
Other comprehensive loss:		
Unrealized holding loss on marketable securities	—	(21)
Comprehensive loss	$ (14,228)	$ (17,247)

See accompanying notes to unaudited condensed consolidated financial statements.

SYROS PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF STOCKHOLDER'S EQUITY
For the three months ended March 31, 2021 and 2020
(in thousands, except share data)
(unaudited)

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Gain (Loss)	Accumulated Deficit	Stockholders' Equity
	Number of Shares	Par Value				
Balance at December 31, 2019	43,367,801	$ 43	$ 372,100	$ 24	$ (292,983)	$ 79,184
Exercise of stock options	30,595	—	100	—	—	100
Vesting of restricted stock units	90,512	—	—	—	—	—
Stock-based compensation expense	—	—	2,459	—	—	2,459
Issuance of common stock at-the-market, net of issuance costs of $411	2,201,810	2	11,917	—	—	11,919
Issuance of warrants	—	—	128	—	—	128
Other comprehensive loss	—	—	—	(21)	—	(21)
Net loss	—	—	—	—	(17,226)	(17,226)
Balance at March 31, 2020	45,690,718	$ 45	$ 386,704	$ 3	$ (310,209)	$ 76,543
Balance at December 31, 2020	56,222,746	$ 56	$ 467,518	$ —	$ (377,021)	$ 90,553
Exercise of stock options	20,134	—	157	—	—	157
Vesting of restricted stock units	206,762	—	—	—	—	—
Stock-based compensation expense	—	—	2,930	—	—	2,930
Issuance of common stock in underwritten public offering, net of issuance costs of $5,132	5,400,000	5	70,463	—	—	70,468
Net loss	—	—	—	—	(14,228)	(14,228)
Balance at March 31, 2021	61,849,642	$ 61	$ 541,068	$ —	$ (391,249)	$ 149,880

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

	Three Months Ended March 31,	
	2021	2020
Operating activities		
Net loss	$ (14,228)	$ (17,226)
Adjustments to reconcile net loss to net cash (used in) provided by operating activities:		
Depreciation and amortization	666	678
Amortization of financing right-of-use asset	65	65
Stock-based compensation expense	2,930	2,459
Change in fair value of warrant liability	(7,670)	—
Net amortization of premiums and discounts on marketable securities	—	(49)
Amortization of debt-discount and accretion of deferred debt costs	167	40
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	329	358
Accounts receivable	7	20,000
Contract assets	(298)	(1,477)
Other long-term assets	(27)	(286)
Accounts payable	63	(1,060)
Accrued expenses	(1,680)	(3,357)
Deferred revenue	(2,134)	(902)
Proceeds for tenant improvement incentive from landlord	—	586
Operating lease asset and liabilities	(180)	417
Net cash (used in) provided by operating activities	(21,990)	246
Investing activities		
Purchases of property and equipment	(262)	(1,797)
Maturities of marketable securities	—	45,000
Net cash (used in) provided by investing activities	(262)	43,203
Financing activities		
Payments on financing and capital lease obligations	(64)	(58)
Proceeds from issuance of common stock through employee benefit plans	157	100
Proceeds from issuance of common stock through at-the-market sales agreement, net of issuance costs	—	11,937
Proceeds from term loan, net of issuance costs	—	19,714
Proceeds from issuance of common stock in public offering, net of issuance costs	70,353	—
Payment of issuance cost related to out of period offering and debt issuance	(36)	—
Net cash provided by financing activities	70,410	31,693
Increase in cash, cash equivalents and restricted cash	48,158	75,142
Cash, cash equivalents and restricted cash (See reconciliation in Note 6)		
Beginning of period	177,070	44,817
End of period	$ 225,228	$ 119,959
Supplemental disclosure of cash flow information:		
Cash paid for interest	$ 789	$ 231
Cash paid for tax	$ —	$ 7
Non-cash investing and financing activities:		
Property and equipment received but unpaid as of period end	$ —	$ 991
Deferred debt financing costs incurred but unpaid as of period end	$ —	$ 10
Offering costs incurred but unpaid as of period end	$ 26	$ 41

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 seeking to redefine the power of small molecules to 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.

On January 22, 2021, the Company issued and sold an aggregate of5,400,000 shares of its common stock in an underwritten public offering at a public offering price of $14.00 per share, resulting in gross proceeds of $75.6 million before deducting underwriting discounts and commissions and other transaction expenses of approximately $5.1 million.

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 $84.0 million, $75.4 million and $62.3 million for the years ended December 31, 2020, 2019 and 2018, respectively. As of March 31, 2021, the Company had an accumulated deficit of $391.2 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, license and collaboration agreements and term debt. The Company has devoted substantially all of its financial resources and efforts to research and development and general and administrative activities 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 and cash equivalents of $222.1 million as of March 31, 2021 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 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, 2020 and notes thereto included in the Company's Annual Report on Form 10-K for the year ended December 31, 2020 filed with the Securities and Exchange Commission ("SEC") on March 4, 2021.

The unaudited interim condensed consolidated financial statements have been prepared on the same basis as the audited financial statements. 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 March 31, 2021, the results of its operations, statements of cash flows and statements of stockholders' equity for the three months ended March 31, 2021 and 2020. Such adjustments are of a normal and recurring nature. The results for the three months ended March 31, 2021 are not necessarily indicative of the results for the year ending December 31, 2021, 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 subsidiaries, Syros Securities Corporation, a Massachusetts corporation formed by the Company in December 2014 to exclusively engage in buying, selling and holding securities on its own behalf, and Syros Pharmaceuticals (Ireland) Limited, an Irish limited liability company formed by the Company in January 2019. 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 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, warrant liability, stock-based compensation expense, accrued expenses and income taxes. Actual results may differ from those estimates or assumptions. The full extent to which the COVID-19 pandemic will directly or indirectly impact the Company's business, results of operations and financial condition, including expenses, reserves and allowances, clinical trials, research and development costs and employee-related amounts, will depend on future developments that are highly uncertain, including as a result of new information that may emerge concerning COVID-19 and the actions taken to contain it or treat it.

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 generally 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 those 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 those that reflect the Company's assumption about the inputs that market participants would use in pricing the asset or liability. These are developed based on the best information available under 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, restricted cash, accounts payable, accrued expenses and deferred revenue approximate their respective fair values due to their short-term nature.

Amortization of Debt Discount and Issuance Costs

Long-term debt is initially recorded at its allocated proceeds, net of discounts and issuance costs. Debt discount and issuance costs, consisting of legal fees, fair value of the warrant at its issuance date and other issuance fees directly related to the debt, are offset against the initial carrying value of the debt and are amortized to interest expense over the estimated life of the debt using the effective interest method.

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.

The Company recognizes revenue in accordance with ASC 606, *Revenue from Contracts with Customers* ("ASC 606"). ASC 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 ASC 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 ASC 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 Company will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. If a contract is determined to be within the scope of ASC 606 at inception, the Company assesses the goods or services promised within such contract, determines which of those goods and services 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.

If the Company performs by transferring goods or services to a customer before the customer pays consideration or before payment is due, the Company records a contract asset, excluding any amounts presented as accounts receivable. The Company includes unbilled accounts receivable as contract assets on its consolidated balance sheets. The Company records accounts receivable for amounts billed to the customer for which the Company has an unconditional right to consideration. The Company assesses contract assets and accounts receivable for impairment and, to date, no impairment losses have been recorded.

From time to time, the Company may enter into agreements that are within the scope of ASC 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 or prepaid research and development services; 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 ASC 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 ASC 606. For those elements of the arrangement that are accounted for pursuant to ASC 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.

Warrants

The Company accounts for issued warrants either as a liability or equity in accordance with ASC 480-10, *Accounting for Certain Financial Instruments with Characteristics of both Liabilities and Equity* ("ASC 480-10") or ASC 815-40, *Accounting for Derivative Financial Instruments Indexed to, and Potentially Settled in, a Company's Own Stock* ("ASC 815-40"). Under ASC 480-10, warrants are considered a liability if they are mandatorily redeemable and they require settlement in cash, other assets, or a variable number of shares. If warrants do not meet liability classification under ASC 480-10, the Company considers the requirements of ASC 815-40 to determine whether the warrants should be classified as a liability or as equity. Under ASC 815-40, contracts that may require settlement for cash are liabilities, regardless of the probability of the occurrence of the triggering event. Liability-classified warrants are measured at fair value on the issuance date and at the end of each reporting period. Any change in the fair value of the warrants after the issuance date is recorded in the consolidated statements of operations as a gain or loss. If warrants do not require liability classification under ASC 815-40, in order to conclude warrants should be classified as equity, the Company assesses whether the warrants are indexed to its common stock and whether the warrants are classified as equity under ASC 815-40 or other applicable GAAP standard. Equity-classified warrants are accounted for at fair value on the issuance date with no changes in fair value recognized after the issuance date.

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 units and stock option awards, to be recognized as expense in the consolidated statements of operations based on their grant date fair values. Consistent with the grants for employees and directors, grants of restricted stock units and stock option awards to other service providers, referred to as non-employees, are measured based on the grant-date fair value of the award and expensed in the Company's condensed consolidated statement of operations over the vesting period. The Company estimates the fair value of stock 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, the Company determines its expected volatility by using a blend of its historical experience and a weighted average of selected peer companies. 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 to non-employees can be determined using either the contractual term of the option award or the "simplified" method. 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 units.

The Company expenses the fair value of its stock-based awards to employees and non-employees on a straight-line basis over the associated service period, which is generally the vesting period. 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.

Compensation expense for discounted purchases under the employee stock purchase plan is measured using the Black-Scholes model to compute the fair value of the lookback provision plus the purchase discount and is recognized as compensation expense over the offering period.

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 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. Compensation expense for such awards is recognized over the six-year vesting period unless management determines that the achievement of any performance-based milestones is probable, in which case expense is accelerated.

Net Loss per Share

Basic net earnings per share applicable to common stockholders is calculated by dividing net earnings applicable to common stockholders by the weighted average shares outstanding during the period, without consideration for common stock equivalents. Diluted net earnings per share applicable to common stockholders 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 calculation of dilutive net loss per share applicable to common stockholders, stock options, unvested restricted stock units, and warrants are considered to be common stock equivalents but are excluded from the calculation of diluted net loss per share applicable to common stockholders, as their effect would be anti-dilutive; therefore, basic and diluted net loss per share applicable to common stockholders were the same for all periods presented.

As of March 31, 2021, pre-funded warrants to purchase1,000,000 shares of common stock that were issued in connection with the December 2020 private placement (refer to Note 10) were included in the basic and diluted net loss per share calculation.

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

	As of March 31,	
	2021	2020
Stock options	6,504,401	5,504,177
Unvested restricted stock units	2,070,150	1,641,346
Warrants*	4,990,156	2,145,642
Total	13,564,707	9,291,165

* As of March 31, 2021, this is comprised of 2,117,094 warrants to purchase common stock issued in connection with the Company's April 2019 financing (refer to Note 10), 27,548 warrants to purchase common stock issued in connection with the execution of the Company's loan agreement in February 2020 (refer to Note 7), 17,389 warrants to purchase common stock issued in connection with the second draw on this loan agreement in December 2020 (refer to Note 7), and 2,828,125 warrants to purchase common stock issued in connection with the private placement in December 2020 (refer to Note 10). As of March 31, 2020, this is comprised of 2,118,094 warrants to purchase common stock issued in connection with the Company's April 2019 financing (refer to Note 10) and 27,548 warrants to purchase common stock issued in connection with the execution of the Company's loan agreement in February 2020 (refer to Note 7).

Income Taxes

The Company accounts for uncertain tax positions using a more-likely-than-not threshold for recognizing and resolving uncertain tax positions. The evaluation of uncertain tax positions is based on factors including, but not limited to, changes in the law, the measurement of tax positions taken or expected to be taken in tax returns, the effective settlement of matters subject to audit, new audit activity, and changes in facts or circumstances related to a tax position.

Recent Accounting Pronouncements

In August 2020, the FASB issued ASU No. 2020-06,*Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity* ("ASU 2020-06"). The amendments in ASU 2020-06 simplify the accounting for certain financial instruments with characteristics of liabilities and equity, including convertible instruments and contracts in an entity's own equity. The standard is effective for public companies for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2021. Early adoption is permitted. The Company is currently evaluating this new standard and does not anticipate that it will have a material impact on its consolidated financial statements and related disclosures.

In April 2019, the FASB issued ASU No. 2019-04,*Codification Improvements to Topic 326 Financial Instruments – Credit Losses, Topic 815, Derivatives and Hedging, and Topic 825* ("ASU 2019-04"). ASU 2019-04 clarifies the accounting treatment for the measurement of credit losses under ASC 236 and provides further clarification on previously issued updates including ASU 2017-12, *Derivatives and Hedging (Topic 815): Targeted Improvements to Accounting for Hedging Activities* and ASU 2016-01, *Financial Instruments—Overall (Subtopic 825-10): Recognition and Measurement of Financial Assets and Financial Liabilities*. ASU 2019-04 is effective for fiscal years beginning after December 15, 2022, including interim periods within those fiscal years. Early adoption is permitted. The Company is currently in the process of evaluating the new standard but does not anticipate ASU 2019-14 will have a material impact on its consolidated financial statements and related disclosures.

3. Collaboration and Research Arrangements

Collaboration with Global Blood Therapeutics

On December 17, 2019, the Company entered into a license and collaboration agreement (the "GBT Collaboration Agreement") with Global Blood Therapeutics, Inc. ("GBT"), pursuant to which the parties agreed to a research collaboration to discover novel targets that induce fetal hemoglobin in order to develop new small molecule treatments for sickle cell disease and beta thalassemia. The research term (the "Research Term") is for an initial period of three years and can be extended for up to two additional one-year terms upon mutual agreement.

Pursuant to the terms of the GBT Collaboration Agreement, GBT paid the Company an upfront payment of $20.0 million. GBT also agreed to reimburse the Company for full-time employee and out-of-pocket costs and expenses incurred by the Company in accordance with the agreed-upon research budget, which is anticipated to total approximately $40.0 million over the initial Research Term.

The Company granted to GBT an option (the "Option") to obtain an exclusive, worldwide license, with the right to sublicense, under relevant intellectual property rights and know-how of the Company arising from the collaboration to develop, manufacture and commercialize any compounds or products resulting from the collaboration GBT may exercise the Option at any time during the period (i) commencing on the earlier of (a) the date of GBT's designation of the first product candidate to enter investigational new drug application-enabling studies, or (b) if no such candidate is designated as of the expiration of the Research Term, the date of expiration of the Research Term, and (ii) ending on the 180th day after the date of expiration or earlier termination of the Research Term. GBT's exercise of the Option will be subject to any required filings with the applicable antitrust authority as required by the antitrust laws and satisfaction of any applicable antitrust conditions.

Should GBT exercise its Option, the Company could receive up to $315.0 million in option exercise, development, regulatory, commercialization and sales-based milestones per product candidate and product resulting from the collaboration.

The Company will also be entitled to receive, subject to certain reductions, tiered mid-to-high single digit royalties as percentages of calendar year net sales on any product.

Either party may terminate the GBT Collaboration Agreement for the other party's uncured material breach or insolvency, and in certain other specified circumstances, subject to specified notice and cure periods. GBT may unilaterally terminate the GBT Collaboration Agreement in its entirety, for any or no reason, upon nine-months' prior written notice to the Company if such notice is delivered during the Research Term, or 90 days' prior written notice to the Company if such notice is delivered after the expiration or termination of the Research Term.

GBT Collaboration Revenue

The Company analyzed the GBT Collaboration Agreement and concluded that it represents a contract with a customer within the scope of ASC 606.

The Company identified a single performance obligation, which includes a (i) non-exclusive research license that GBT will have access to during the initial Research Term and (ii) research and development services provided during the initial Research Term. The GBT Collaboration Agreement includes the Option. The Option does not provide a material right to GBT that it would receive without entering into the GBT Collaboration Agreement, principally because the Option exercise fee is at least equal to the standalone selling price for the underlying goods. The non-exclusive research license is not distinct as GBT cannot benefit from the license without the research and development services that are separately identifiable in the contract. The non-exclusive research license only allows GBT to evaluate the candidate compounds developed under the research plan or to conduct work allocated to it during the Research Term. GBT cannot extract any benefit from the non-exclusive research license without the research and development services performed by the Company, including the provision of data package information. As such, these two promises are inputs to a combined output (the delivery of data package allowing GBT to make an Option exercise decision) and are bundled into a single performance obligation (the non-exclusive research license and research and development service performance obligation).

At inception, the total transaction price was determined to be approximately $60.0 million, which consisted of a $20.0 million upfront non-refundable and non-creditable technology access fee and approximately $40.0 million in reimbursable costs for employee and external research and development expenses. The GBT Collaboration Agreement also provides for development and regulatory milestones which are only payable subsequent to the exercise of the Option, and therefore are excluded from the transaction price at inception. The Company will re-evaluate the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur.

During the three months ended March 31, 2021, there was no change in the total transaction price, which remained at approximately $60.0 million.

ASC 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 non-exclusive research license and research and development 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 GBT receives the benefit of the services, as the overall purpose of the arrangement is for the Company to perform the services. The Company will recognize revenue associated with the performance obligation as the research

and development services are provided using an input method, according to the costs incurred as related to the research and development activities and the costs expected to be incurred in the future to satisfy the performance obligation. The transfer of control occurs during this time and is the best measure of progress towards satisfying the performance obligation.

During the three months ended March 31, 2021 and 2020, the Company recognized revenue of $4.0 million and $2.2 million, respectively, under the GBT Collaboration Agreement. As of March 31, 2021, the Company has deferred revenue outstanding under the GBT Collaboration Agreement of approximately $15.4 million, of which $8.8 million and $6.6 million were classified as deferred revenue, current portion and deferred revenue, net of current portion, respectively, on the Company's condensed consolidated balance sheets.

Agreements with Incyte Corporation

In January 2018, the Company and Incyte entered into a Target Discovery, Research Collaboration and Option Agreement (the "Incyte Collaboration Agreement"). The Incyte Collaboration Agreement was amended in November 2019. Under the Incyte 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. For each option exercised by Incyte, Incyte will have the exclusive worldwide right to use the licensed intellectual property to develop and commercialize therapeutic products that modulate the target as to which the option was exercised. Under the terms of the Incyte 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 Incyte 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 Prepaid Research Amount.

In January 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 a 30% premium over the volume-weighted sale price of the shares of the Company's common stock over the 15-trading day period immediately preceding the date of the Stock Purchase Agreement.

Incyte Collaboration Revenue

The Company analyzed the Incyte Collaboration Agreement and concluded that it represents a contract with a customer within the scope of ASC 606.

The Company identified a single performance obligation which includes (i) a 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 Incyte 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.

At inception, the total transaction price was determined to be $12.3 million and was subsequently increased to $12.8 million following a November 2019 amendment. As of March 31, 2021, the total transaction price is $12.8 million, consisting of a $2.5 million upfront non-refundable and non-creditable payment, the $7.5 million Prepaid Research Amount, $2.3 million in premium paid on the equity investment made pursuant the Stock Purchase Agreement, and $0.5 million of additional consideration. The Company accounted for the contract amendment as a modification as if it were part of the existing contract as the remaining goods and services are not distinct, and therefore form part of a single performance obligation that was partially satisfied at the date of the amendment. This additional consideration is recognized on a percent complete basis as work is performed.

The Incyte 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 the transaction price at inception. The Company re-evaluates the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur.

The Company recognizes revenue associated with the performance obligation as the research and development services are provided using an input method, according to the costs incurred as related to the research and development activities and the costs expected to be incurred in the future to satisfy the performance obligation. The transfer of control occurs during this time and is the best measure of progress towards satisfying the performance obligation.

During the three months ended March 31, 2021 and 2020, the Company recognized $0.8 million and $0.2 million of revenue, respectively, under the Incyte Collaboration Agreement. As of March 31, 2021, the Company has deferred revenue outstanding under the Incyte Collaboration Agreement of approximately $4.6 million, of which $4.0 million and $0.6 million were classified as deferred revenue, current portion and deferred revenue, net of current portion, respectively, on the Company's condensed consolidated balance sheets.

The following table presents the changes in accounts receivable, contract assets and liabilities for the three months ended March 31, 2021 (in thousands):

	Balance at December 31, 2020	Additions	Deductions	Balance at March 31, 2021
Accounts receivable and contract assets:				
Billed receivables from collaboration partners	$ 7	$ 2,397	$ (2,404)	$ —
Unbilled receivables from collaboration partners	2,324	2,622	(2,324)	2,622
Total accounts receivable and contract assets	$ 2,331	$ 5,019	$ (4,728)	$ 2,622
Contract liabilities:				
Deferred revenue - Incyte	$ 5,365	$ —	$ (809)	$ 4,556
Deferred revenue - GBT	16,721	71	(1,396)	15,396
Total contract liabilities	$ 22,086	$ 71	$ (2,205)	$ 19,952

4. Cash and Cash Equivalents

Cash equivalents are highly liquid investments that are readily convertible into cash with original maturities of three months or less when purchased. Unrealized gains or losses are included in accumulated other comprehensive gain (loss). Premiums or discounts from par value are amortized to other (expense) income over the life of the underlying security.

Cash and cash equivalents consisted of the following at March 31, 2021 and December 31, 2020 (in thousands):

March 31, 2021	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Cash and cash equivalents:				
Cash and money market funds	$ 222,142	$ —	$ —	$ 222,142
Total:	$ 222,142	$ —	$ —	$ 222,142

December 31, 2020	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Cash and cash equivalents:				
Cash and money market funds	$ 173,984	$ —	$ —	$ 173,984
Total:	$ 173,984	$ —	$ —	$ 173,984

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 months ended March 31, 2021 and 2020, there were no realized gains or losses on sales of investments, and no investments were adjusted for other-than-temporary declines in fair value.

5. Fair Value Measurements

Assets and liabilities measured at fair value on a recurring basis as of March 31, 2021 and December 31, 2020 were as follows (in thousands):

Description	March 31, 2021	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Assets:				
Cash	$ 130,737	$ 130,737	$ —	$ —
Money market funds	91,405	91,405	—	—
	$ 222,142	$ 222,142	$ —	$ —
Liabilities:				
Warrant liability	$ 12,041	$ —	$ —	$ 12,041
	$ 12,041	$ —	$ —	$ 12,041

Description	December 31, 2020	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Assets:				
Cash	$ 47,579	$ 47,579	$ —	$ —
Money market funds	126,405	126,405	—	—
	$ 173,984	$ 173,984	$ —	$ —
Liabilities:				
Warrant liability	$ 19,711	$ —	$ —	$ 19,711
	$ 19,711	$ —	$ —	$ 19,711

Assumptions Used in Determining Fair Value of Warrants

The Company issued warrants to purchase an aggregate of up to2,828,125 shares of common stock in connection with a private placement on December 8, 2020 (see Note 10) (the "Warrants"). In the event of certain fundamental transactions involving the Company, the Warrant holders may require the Company to make a payment based on a Black-Scholes valuation, using specified inputs; therefore, the Warrants were accounted for as liabilities. The Company recorded the fair value of the Warrants upon issuance using the Black-Scholes valuation model and is required to revalue the Warrants at each reporting date with any changes in fair value recorded on our statement of operations. The valuation of the Warrants is considered under Level 3 of the fair value hierarchy and influenced by the fair value of the underlying common stock of the Company.

A summary of the Black Scholes pricing model assumptions used to record the fair value of the Warrants is as follows:

	March 31, 2021	December 31, 2020
Risk-free interest rate	0.83 %	0.35 %
Dividend yield	—	—
Expected life (in years)	4.69	4.94
Expected volatility	83.57 %	82.66 %

Changes in Level 3 Liabilities Measured at Fair Value on a Recurring Basis

The following table reflects the change in the Company's Level 3 Warrant liability for the three months ended March 31, 2021 (in thousands):

	Warrant liability
Fair value as of December 31, 2020	$ 19,711
Change in fair value	(7,670)
Fair value as of March 31, 2021	$ 12,041

As of March 31, 2021, the fair value of the long-term debt is based on Level 3 inputs and approximated its carrying value.

6. Restricted Cash

At March 31, 2021 and December 31, 2020, the Company had $3.1 million in restricted cash, all of which was classified as long-term on the Company's condensed consolidated balance sheets, and all of which was attributable to the 2019 Lease (See Note 9).

In connection with the execution of the 2019 Lease, the Company was required to provide the landlord with a letter of credit in the amount of $3.1 million that will expire 95 days after expiration or early termination of the 2019 Lease. The Company will have the right, under certain conditions, to reduce the amount of the letter of credit to $2.1 million in October 2023.

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 Company's condensed consolidated statement of cash flows as of March 31, 2021, December 31, 2020, March 31, 2020 and December 31, 2019 (in thousands):

	March 31, 2021	December 31, 2020	March 31, 2020	December 31, 2019
Cash and cash equivalents	$ 222,142	$ 173,984	$ 116,873	$ 41,441
Restricted cash, current portion	—	—	—	290
Restricted cash, net of current portion	3,086	3,086	3,086	3,086
Total cash, cash equivalents and restricted cash	$ 225,228	$ 177,070	$ 119,959	$ 44,817

7. Oxford Finance Loan Agreement

On February 12, 2020, the Company entered into a Loan and Security Agreement (the "Loan Agreement") with Oxford Finance LLC (the "Lender"). Pursuant to the Loan Agreement, a term loan of up to an aggregate principal amount of $60.0 million is available to the Company. A first tranche term loan for $20.0 million was funded on February 12, 2020, and a second tranche term loan for $20.0 million was funded on December 23, 2020. The remaining $20.0 million is still available under the Loan Agreement, at the sole discretion of the Lender.

The term loan bears interest at an annual rate equal to the greater of (i) 7.75% and (ii) the sum of 5.98% and the greater of (A) one-month LIBOR or (B) 1.77%. The Loan Agreement provides for interest-only payments until March 1, 2023, and repayment of the aggregate outstanding principal balance of the term loan in monthly installments starting on March 1, 2023 and continuing through February 1, 2025 (the "Maturity Date"). The Company paid a facility fee of $0.1 million upon the funding of the first tranche, paid a facility fee of $75,000 upon funding of the second tranche and must pay a $50,000 facility fee if and when the third loan tranche is funded. The Company will be required to make a final payment fee of 5.00% of the amount of the term loan drawn payable on the earlier of (i) the prepayment of the term loan or (ii) the Maturity Date. At the Company's option, the Company may elect to prepay the loans subject to a prepayment fee equal to the following percentage of the principal amount being prepaid: 2% if an advance is prepaid during the first 12 months following the applicable advance date, 1% if an advance is prepaid after 12 months but prior to 24 months following the applicable advance date, and 0.5% if an advance is prepaid any time after 24 months following the applicable advance date but prior to the Maturity Date.

In connection with the Loan Agreement, the Company granted the Lender a security interest in all of the Company's personal property now owned or hereafter acquired, excluding intellectual property (but including the right to payments and proceeds of intellectual property), and a negative pledge on intellectual property. The Loan Agreement also contains certain events of default, representations, warranties and non-financial covenants of the Company.

In connection with the funding of the first tranche in February 2020, the Company issued the Lender warrants to purchase 27,548 shares of the Company's common stock at an exercise price per share of $7.26. In connection with the funding of the second tranche in December 2020, the Company issued the Lender warrants to purchase 17,389 shares of the Company's common stock at an exercise price of $11.50 per share (collectively, the "Oxford Warrants"). The Oxford Warrants are exercisable within five years from their respective dates of issuance.

The Oxford Warrants are classified as a component of permanent equity because they are freestanding financial instruments that are legally detachable and separately exercisable from the shares of common stock with which they were issued, are immediately exercisable, do not embody an obligation for the Company to repurchase its shares, and permit the holders to receive a fixed number of shares of common stock upon exercise. In addition, the Oxford Warrants do not provide any guarantee of value or return. The Company valued the Oxford Warrants at issuance using the Black-Scholes option pricing model and determined the fair value of the Oxford Warrants to be $0.1 million for the first tranche and $0.2 million for the second tranche. The key inputs to the valuation model included an average volatility of 75.43% for the first tranche and 82.41% for the second tranche, and an expected term of 5.0 years for both tranches.

The Company has the following minimum aggregate future loan payments as of March 31, 2021 (in thousands):

Nine months ending December 31, 2021	$ —
Year ended December 31, 2022	—
Year ended December 31, 2023	16,666
Year ended December 31, 2024	20,000
Year ended December 31, 2025	3,334
Total minimum payments	$ 40,000
Less unamortized debt discount	(600)
Plus accumulated accretion of final fees	318
Less current portion	—
Long-term debt, net of current portion	$ 39,718

For the three months ended March 31, 2021, interest expense related to the Loan Agreement was approximately $0.9 million. The total carrying value of debt is classified as long-term on the Company's condensed consolidated balance sheets as of March 31, 2021.

8. Accrued Expenses

Accrued expenses consisted of the following as of March 31, 2021 and December 31, 2020 (in thousands):

	March 31, 2021	December 31, 2020
External research and preclinical development	$ 6,367	$ 4,702
Employee compensation and benefits	2,180	5,715
Professional fees	503	602
Facilities and other	77	65
	$ 9,127	$ 11,084

9. Commitments and Contingencies

Operating Lease

On January 8, 2019, the Company entered into a lease (the "2019 Lease") with respect to approximately 52,859 square feet of space in Cambridge, Massachusetts for a lease term commencing in January 2019 and ending in February 2030. The Company has the option to extend the lease term for one additional ten-year period. The 2019 Lease has escalating rent payments and the Company records rent expense on a straight-line basis over the term of the 2019 Lease, including any rent-free periods. The 2019 Lease includes certain lease incentives in the form of tenant allowances. The 2019 Lease also included an abatement period during which the Company was not required to remit monthly rent payments until March 2020.

In connection with the execution of the 2019 Lease, the Company was required to provide the landlord with a letter of credit in the amount of $3.1 million (See Note 6).

The Company determined that, for purposes of applying the lease accounting guidance codified in ASU No. 2016-02 *Leases (Topic 842) (*"ASC 842"), the commencement date of the 2019 Lease occurred on May 1, 2019. The Company recorded a right-of-use asset and lease liability of $15.8 million using an incremental borrowing rate of 9.3%, net of tenant allowances expected to be received of $9.3 million, on the May 1, 2019 lease commencement date. The Company is amortizing the tenant allowance to offset rent expenses over the term of the 2019 Lease starting at the lease commencement date on a straight-line basis. On the Company's condensed consolidated balance sheets, the Company classified $1.5 million of the lease liability as short-term and $24.2 million of the lease liability as long-term as of March 31, 2021.

The Company elected the practical expedient provided under ASC 842 and therefore combined all lease and non-lease components when determining the right-of-use asset and lease liability for the 2019 Lease.

Financing Lease

In March 2019, the Company entered into an equipment lease agreement (the "Equipment Lease") that has a 48-month term. At the end of the term, the Company has the right to return the leased equipment, extend the lease, or buy the equipment at the then-current fair market value of the equipment. The Company accounted for the Equipment Lease as a financing lease under ASC 842 and recorded a financing lease right-of-use asset and a corresponding financing lease liability of approximately $1.0 million at the time the Equipment Lease was executed.

The following is a maturity analysis of the annual undiscounted cash flows reconciled to the carrying value of the operating and financing lease liabilities as of March 31, 2021 (in thousands):

	Operating	Financing
Nine months ending December 31, 2021	$ 2,873	$ 234
Year ended December 31, 2022	3,935	313
Year ended December 31, 2023	4,049	66
Year ended December 31, 2024	4,166	—
Year ended December 31, 2025 and beyond	23,543	—
Total minimum lease payments	38,566	613
Less imputed interest	(12,874)	(56)
Total lease liability	$ 25,692	$ 557

The following table outlines the total lease cost for the Company's operating and financing leases as well as weighted average information for these leases as of March 31, 2021 (in thousands):

	Three Months Ended March 31, 2021
Lease cost:	
Operating lease cost	$ 772
Financing lease cost:	
Amortization of right-of-use asset	$ 65
Interest on lease liabilities	14
Total financing lease cost	$ 79
Cash paid for amounts included in the measurement of liabilities:	
Operating cash flows from operating lease	$ 951
Operating cash flows from financing lease	$ 78

Other information:	Three Months Ended March 31, 2021
Weighted-average remaining lease term (in years) - operating lease	8.92
Weighted-average discount rate - operating lease	9.30 %
Weighted-average remaining lease term (in years) - financing lease	2.06
Weighted-average discount rate - financing lease	9.47 %

Following the adoption of ASC 842, the Company has a right-of-use asset and lease liability that results in recording a temporary tax difference. This temporary tax difference is the result of recognizing a right-of-use asset and related lease liability while such asset and liability have no corresponding tax basis.

Asset Purchase Agreement

Orsenix, LLC

On December 4, 2020, the Company entered into an asset purchase agreement (the "Asset Purchase Agreement") with Orsenix, LLC ("Orsenix"), pursuant to which the Company acquired Orsenix's assets related to a novel oral form of arsenic trioxide, which the Company refers to as SY-2101. Under the terms of the Asset Purchase Agreement, the Company paid an up-front fee of $12.0 million in cash upon closing of the transaction and is required to pay to Orsenix:

- single-digit million milestone payments related to the development of SY-2101 in indications other than acute promyelocytic leukemia ("APL");
- $6.0 million following the achievement of a regulatory milestone related to the development of SY-2101 in APL; and
- up to $10.0 million upon the achievement of certain commercial milestones with respect to SY-2101.

The Company's obligation to pay the commercial milestone payments expires following the tenth anniversary of the first commercial sale of SY-2101. The Asset Purchase Agreement requires the Company to use commercially reasonable efforts to develop and commercialize SY-2101 for APL in the United States during such period, and to use commercially reasonable efforts to dose the first patient in a Phase 3 clinical trial of SY-2101 on or before the third anniversary of the closing of the transaction; however, the Company retains sole discretion to operate the acquired assets as it determines. The assets acquired from Orsenix do not meet the definition of a business under ASC 805 "*Business Combinations"* ("ASC 805") because substantially all of the fair value of the assets acquired is concentrated in a single identifiable asset, the rights to SY-2101. Furthermore, as the acquired asset does not include a substantive process, the asset does not meet the minimum requirements to be considered a business under ASC 805. As SY-2101 does not have an alternative future use, the Company recorded the $12.0 million upfront cash payment as research and development expense on the date of acquisition in December 2020. The Company will expense any future milestone payments made prior to the time an alternative future use for SY-2101 has been established. Once an alternative future use for SY-2101 has been established, the Company will capitalize milestone payments as an addition to the carrying value of SY-2101.

License Agreements

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, and further amended in January 2021 to expand the territory under which the Company is licensed to include Central and South America, Australia, Israel, and Russia.

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 incurred fees of $0.3 million under this supply management agreement during the three months ended March 31, 2020. No fees were incurred under this supply management agreement during the three months ended March 31, 2021.

10. Stockholders' equity

Issuance of Securities through an Underwritten Public Offering

On January 22, 2021, the Company issued and sold an aggregate of5,400,000 shares of its common stock in an underwritten public offering at a public offering price of $14.00 per share, resulting in gross proceeds of $75.6 million before deducting underwriting discounts and commissions and other transaction expenses of approximately $5.1 million. The public offering was made pursuant to an underwriting agreement entered into by the Company with Cowen and Company, LLC and Piper Sandler & Co., as representatives of the several underwriters, on January 19, 2021. The shares were issued pursuant to a shelf registration statement on Form S-3 that was filed with the SEC on June 12, 2020 and declared effective by the SEC on June 22, 2020.

Issuance of Securities through a Private Placement

On December 8, 2020, the Company issued in a private placement10,312,500 shares of common stock, and, in lieu of shares of common stock, pre-funded warrants (the "Pre-Funded Warrants") to purchase an aggregate of 1,000,000 shares of common stock, and, in each case, accompanying Warrants to purchase an aggregate of up to 2,828,125 additional shares of common stock (or Pre-Funded Warrants to purchase common stock in lieu thereof) at a price of $8.00 per share and accompanying Warrant (or $7.99 per Pre-Funded Warrant and accompanying Warrant). The private placement resulted in aggregate gross proceeds of $90.5 million, before $0.4 million of transaction costs.

In the event of certain fundamental transactions involving the Company, the holders of Warrants may require the Company to make a payment based on a Black-Scholes valuation, using specified inputs. The holders of Pre-Funded Warrants do not have similar rights. Therefore, the Company accounted for the Warrants as liabilities, while the Pre-Funded Warrants met the permanent equity criteria classification. The Pre-Funded Warrants are classified as a component of permanent equity because they are freestanding financial instruments that are legally detachable and separately exercisable from the shares of common stock with which they were issued, are immediately exercisable, do not embody an obligation for the Company to repurchase its shares, and permit the holders to receive a fixed number of shares of common stock upon exercise. In addition, the Pre-Funded Warrants do not provide any guarantee of value or return. The initial fair value of the Warrants at issuance was $19.3 million, determined using the Black-Scholes valuation model. The Company remeasured the Warrants' fair value at March 31, 2021 and December 31, 2020 as $12.0 million and $19.7 million, respectively. The change in fair value of $7.7 million during the three months ended on March 31, 2021 was recorded in the condensed statement of operations for the three months ended March 31, 2021.

Convertible Preferred Stock and 2019 Warrants

On April 9, 2019, the Company completed two concurrent underwritten public offerings of its equity securities. In the first public offering, the Company sold 8,667,333 shares of its common stock and accompanying Class A warrants (the "2019 Warrants") to purchase1,951,844 shares of the Company's common stock at a combined price to the public of $7.50 per common share and accompanying 2019 Warrant. In the second public offering, the Company sold666 shares of its Series A convertible preferred stock (the "Series A Preferred Stock") and accompanying 2019 Warrants to purchase 166,500 shares of the Company's common stock at a combined public offering price of $7,500 per share and accompanying 2019 Warrant. The offerings resulted in aggregate gross proceeds to the Company of $70.0 million, before underwriting discounts and commissions and offering expenses payable by the Company of approximately $5.0 million.

In November 2019, all 666 shares of Series A Preferred Stock were converted by the holder into666,000 shares of common stock. As of March 31, 2021, there were no shares of Series A Preferred Stock outstanding.

Each 2019 Warrant has an exercise price per share of common stock of $8.625, subject to adjustment in certain circumstances, and will expire onOctober 10, 2022. Each 2019 Warrant is immediately exercisable, provided that the holder is prohibited, subject to certain exceptions, from exercising the 2019 Warrant for shares of the Company's common stock to the extent that immediately prior to or after giving effect to such exercise, the holder, together with its affiliates and other attribution parties, would own more than 4.99% of the total number of shares of the Company's common stock

then issued and outstanding. This percentage may be changed at the holders' election to a higher or lower percentage upon 61 days' notice to the Company.

The Company evaluated the Series A Preferred Stock and 2019 Warrants for liability or equity classification in accordance with the provisions of ASC 480, *Distinguishing Liabilities from Equity*, and determined that equity treatment was appropriate because neither the Series A Preferred Stock nor the 2019 Warrants met the definition of liability instruments.

The 2019 Warrants are classified as a component of permanent equity because they are freestanding financial instruments that are legally detachable and separately exercisable from the shares of common stock with which they were issued, are immediately exercisable, do not embody an obligation for the Company to repurchase its shares, and permit the holders to receive a fixed number of shares of common stock upon exercise. In addition, the 2019 Warrants do not provide any guarantee of value or return. The Company valued the 2019 Warrants at issuance using the Black-Scholes option pricing model and determined the fair value of the 2019 Warrants to purchase 2,118,344 shares of the Company's common stock was $9.0 million. The key inputs to the valuation model included an average volatility of 86.06% and an expected term of 3.5 years.

As of March 31, 2021, 2019 Warrants to purchase 2,117,094 shares of common stock are outstanding and remain unexercised.

11. 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, 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, 2021, the number of shares reserved for issuance under the 2016 Plan was increased by 1,600,000 shares. At March 31, 2021, 1,978,485 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.

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, 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, 2021, the number of shares reserved for issuance under the 2016 ESPP was increased by 562,227 shares. At March 31, 2021, 2,331,383 shares remained available for future issuance under the 2016 ESPP.

Stock Options

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 have a contractual term of ten years from the grant date.

The Company has granted certain 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 for the Company's product candidates 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. As of December 31, 2020, all performance-based milestone related to these stock options were achieved The Company did not record any additional stock-based compensation expense related to the achievement of performance-based milestones during the three months ended March 31, 2021 and 2020.

The Company has granted options to purchase 75,000 shares of common stock to an advisor that vest solely upon the achievement of performance-based criteria. As of March 31, 2021, none of such performance-based criteria had been achieved. As of March 31, 2021, there was $0.3 million of unrecognized compensation cost related to this option, with a remaining contractual period of 5.5 years.

A summary of the status of stock options as of December 31, 2020 and March 31, 2021 and changes during the three months ended March 31, 2021 is presented below:

	Shares	Weighted Average Exercise Price	Remaining Contractual Life (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2020	5,468,605	$ 8.90	7.2	$ 13,124
Granted	1,059,600	11.34		
Exercised	(20,134)	7.77		
Cancelled	(3,670)	9.69		
Outstanding at March 31, 2021	6,504,401	$ 9.30	6.8	$ 3,056
Exercisable at March 31, 2021	3,754,472	$ 9.24	5.9	$ 2,628

The intrinsic value of stock options exercised during the three months ended March 31, 2021 and 2020 was $0.1 million and $0.1 million, respectively.

As of March 31, 2021, there was $17.1 million of total unrecognized compensation cost related to non-vested stock options granted to employees, which is expected to be recognized over a weighted-average period of 2.9 years.

Restricted Stock Units

From time to time, upon approval by the Company's board of directors, certain employees have been granted restricted stock units with time-based vesting criteria. The majority of these restricted stock units vest annually over a four-year term with 25% vesting on each anniversary of the grant date. Restricted stock units granted to the Company's executive officers vest in full three-years from the date of grant. The fair value of restricted stock units is calculated based on the closing sale price of the Company's common stock on the date of grant.

A summary of the status of restricted stock units as of December 31, 2020 and March 31, 2021 and changes during the three months ended March 31, 2021 is presented below:

	Shares	Weighted Average Grant Date Fair Value
Outstanding at December 31, 2020	1,734,383	$ 7.40
Granted	570,204	10.80
Vested	(206,762)	7.23
Forfeited	(27,675)	8.11
Outstanding at March 31, 2021	2,070,150	$ 8.34

As of March 31, 2021, there was $13.5 million of unrecognized stock-based compensation expense related to outstanding restricted stock units, with an expected recognition period of 2.6 years.

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 March 31,	
	2021	2020
Weighted-average risk-free interest rate	0.78%	1.48%
Expected dividend yield	—%	—%
Expected option term (in years)	6.08	6.08
Volatility	82.10%	77.93%

The weighted-average grant date fair value per share of options granted in the three months ended March 31, 2021 and 2020 was $7.89 and $5.11, respectively.

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

	Three Months Ended March 31,	
	2021	2020
Research and development	$ 1,323	$ 1,049
General and administrative	1,607	1,410
Total stock-based compensation expense	$ 2,930	$ 2,459

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, 2020 that we filed with the Securities and Exchange Commission, or SEC, on March 4, 2021, or the 2020 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 also be considered in light of risks identified under the caption "Risk Factors" in the 2020 10-K and in this Quarterly Report on Form 10-Q. We caution you 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 seeking to redefine the power of small molecules to control the expression of genes. Based on our unique ability to elucidate regulatory regions of the genome, we aim to develop medicines that provide a profound benefit for patients with diseases that have eluded other genomics-based approaches. We are currently focused on developing treatments for cancer and diseases resulting from mutations of a single gene, also known as monogenic diseases, and building a clinical stage pipeline of gene control medicines.

Our lead product candidates are:

- SY-1425, a selective retinoic acid receptor alpha, or RARα, agonist that we are evaluating in a Phase 3 clinical trial in combination with azacitidine in a genomically defined subset of patients with higher-risk myelodysplastic syndrome, or HR-MDS, and that we plan to evaluate in a randomized Phase 2 clinical trial in combination with venetoclax and azacitidine in a genomically defined subset of newly diagnosed patients with acute myeloid leukemia, or AML, who are not suitable candidates for standard intensive chemotherapy;
- SY-2101, a novel oral form of arsenic trioxide, or ATO, which we plan to evaluate in a dose confirmation study, followed by a Phase 3 clinical trial, in patients with newly diagnosed acute promyelocytic leukemia, or APL; and
- SY-5609, a highly selective and potent oral inhibitor of cyclin-dependent kinase 7, or CDK7, that we are currently evaluating in the dose escalation portion of a Phase 1 clinical trial in patients with select advanced solid tumors.

We also have multiple preclinical and discovery programs in oncology including our CDK12 inhibitor program (our most advanced program in preclinical development), and programs targeting monogenic diseases such as sickle cell disease and myotonic dystrophy type 1. We expect to nominate our next development candidate to enter investigational new drug application, or IND, enabling preclinical studies in 2022.

In December 2019, we entered into a collaboration with Global Blood Therapeutics, Inc., or GBT, to discover, develop and commercialize novel therapies for sickle cell disease and beta thalassemia. We also 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.

At the 62nd American Society of Hematology Annual Meeting and Exposition held in December 2020, or ASH 2020, we presented new data from our fully enrolled Phase 2 clinical trial evaluating the safety and efficacy of SY-1425 in combination with azacitidine in newly diagnosed AML patients who are not suitable candidates for standard chemotherapy, as well as in relapsed or refractory, or R/R, AML patients who have been prospectively selected using our proprietary RARA, the gene that codes for RARα biomarker. As of an October 1, 2020 data cut-off, 51 newly diagnosed unfit AML patients, including both RARA-positive and RARA-negative patients, were eligible for a safety analysis. Among these patients, SY-1425 in combination with azacitidine was generally well-tolerated, with no evidence of increased toxicity relative to either as a single agent, including rates of myelosuppression that were comparable to single-agent azacitidine. As of the data cut-off, of the 18 RARA-positive patients that were evaluable for clinical response, the overall response rate, or ORR, was 67%, with a composite complete response rate of 61%, with 50% of patients achieving complete response, or CR, and 11% achieving a complete response with incomplete blood count recovery, or CRi. The median time to initial response was 1.2 months, the median duration of response was 10.8 months, and the median overall survival, or OS, among patients who achieved a CR or CRi was 18 months. As of the data cut-off, of the 28 RARA-negative patients that were evaluable for clinical response, the ORR was 43%, with a composite complete response rate of 32%, with 25% of patients achieving CR and 7% achieving CRi. The median time to initial response was 3.0 months, and the median duration of response was 10.3 months. We also presented new translational data demonstrating that most RARA-positive newly diagnosed unfit AML patients have a monocytic disease phenotype that is highly correlated with resistance to upfront treatment with venetoclax and azacitidine. These data suggest that the RARA biomarker not only selects for patients who are more likely to respond to treatment with SY-1425 but also for patients who are less likely to respond to treatment with venetoclax and azacitidine. Approximately 18,000 patients are diagnosed with unfit AML in the United States and Europe annually and we expect the overall total addressable market opportunity for AML to grow to be in excess of $2 billion by 2029. At ASH 2020, we also announced that SY-1425 in combination with azacitidine was generally well-tolerated in the R/R AML patient population. Among the 21 R/R AML patients who were evaluable for clinical response as of the data cut-off, the ORR was 19%, and the median OS was 5.9 months. In hypomethylating agent, or HMA, and venetoclax naïve patients, the ORR was 43%.

Based on these data and our assessment of ongoing areas of high unmet need, we are advancing SY-1425 in combination with azacitidine into a registration-enabling Phase 3 clinical trial in RARA-positive newly diagnosed HR-MDS patients. HR-MDS is a hematologic malignancy that is closely related to AML, and as in AML, about 30% of HR-MDS patients are RARA-positive. Approximately 15,000 patients are diagnosed with HR-MDS in the United States and Europe annually and we expect the total addressable market opportunity for HR-MDS to grow to be in excess of $1 billion by 2029. We plan to enroll approximately 190 RARA-positive newly diagnosed HR-MDS patients in the double-blind placebo-controlled trial, randomized 2:1 to receive SY-1425 in combination with azacitidine or placebo with azacitidine, respectively. The primary endpoint of the trial will be the CR rate. We have begun dosing patients in the Phase 3 clinical trial, and if the trial is successful, we intend to submit to the U.S. Food and Drug Administration, or FDA, a new drug application, or NDA, as early as 2024. In addition, we plan to advance SY-1425 in combination with venetoclax and azacitidine in RARA-positive newly diagnosed unfit AML patients. The trial is designed with a single-arm safety lead-in to confirm the dosing regimen of the triplet to be used in the randomized portion of the Phase 2 clinical trial, which will evaluate the safety and efficacy of SY-1425 in combination with venetoclax and azacitidine compared to venetoclax and azacitidine in approximately 80 patients randomized 1:1. The primary endpoint of the trial will be the composite CR rate. The trial will also evaluate the triplet as a salvage therapy in patients who do not respond to venetoclax and azacitidine. We expect to initiate the Phase 2 clinical trial in the second half of 2021, and we expect to report initial data from the trial in 2022.

In December 2020, we acquired from Orsenix, LLC, or Orsenix, a novel oral form of ATO, which we refer to as SY-2101. SY-2101 is in development for the treatment of APL, a subtype of AML defined by a fusion of the RARA and promyelocytic leukemia, or PML, genes. Approximately 2,000 patients are diagnosed with APL in the United States and Europe annually, representing a potential total addressable market opportunity for APL of approximately $250 million based on current pricing estimates. An intravenously administered, or IV, formulation of ATO is approved for use in combination with All-Trans-Retinoic-Acid, or ATRA, in patients with newly diagnosed APL and, while curative in more than 80% of patients, its administration requires up to 140 two- to four-hour infusions over the typical course of induction and consolidation treatment. Because SY-2101 is dosed orally once daily, we believe it has the potential to become the standard-of-care frontline therapy for APL by providing comparable efficacy with a substantially more convenient option that reduces the treatment burden on patients, improving access, and lowering costs to the healthcare system. In a Phase 1 clinical trial, SY-2101 demonstrated bioavailability, pharmacokinetic, or PK, exposures similar to IV ATO, and a generally well-tolerated safety profile. We plan to initiate a dose confirmation study of SY-2101 in the second half of 2021 and anticipate reporting confirmatory dose and PK data in the first half of 2022. Following confirmation of a dose that

demonstrates comparable PK to IV ATO, we intend to initiate a registration-enabling Phase 3 clinical trial in patients with newly diagnosed APL in 2022 which, if successful, could enable us to submit an NDA as early as 2024.

In January 2020, we dosed the first patient in a Phase 1 clinical trial of SY-5609 in patients with select advanced solid tumors, including breast, colorectal, lung, ovarian and pancreatic cancers, and in solid tumors of any histology having retinoblastoma-pathway, or Rb pathway, alterations. The primary objectives of this trial are to assess the safety and tolerability of escalating doses of SY-5609, with the goal of establishing a maximum tolerated dose. Additional objectives include assessments of anti-tumor activity, PK, pharmacodynamics, or PD, and potential predictive biomarkers, including Rb pathway alterations. In June 2020, we began enrolling patients in a trial cohort assessing the safety of escalating doses of SY-5609 in combination with fulvestrant in HR-positive/HER2-negative metastatic breast cancer patients who have progressed after treatment with a CDK4/6 inhibitor. In a future expansion portion of the Phase 1 clinical trial, multiple cohorts are planned to further evaluate the safety and anti-tumor activity of SY-5609 as both a single agent and in combination with other therapies.

At the 32nd EORTC-NCI-AACR Molecular Targets and Cancer Therapeutics Symposium held in October 2020, or ENA 2020, we reported initial safety, PK, and PD data from the ongoing Phase 1 study of SY-5609. These data demonstrated proof of mechanism and support our ongoing development of SY-5609 for difficult-to-treat cancers. As of an August 21, 2020 data cut-off, 17 patients had been enrolled in the trial and were eligible for safety, PK and PD analysis. Patients were either treated with continuous daily dosing of single-agent SY-5609 at 1, 3, 4 or 5 mg, or for three weeks on and one week off at 3 mg in combination with fulvestrant. The data showed that SY-5609 demonstrated dose-dependent increases in POLR2A mRNA expression, a PD marker being used in the trial to measure CDK7 biological activity. Notably, increases in POLR2A in patients treated at 3 mg daily reached levels associated with tumor regressions in preclinical models, as well as with levels of CDK7 target engagement at which a clinical response and apoptosis were observed in a trial of patients treated with SY-1365, an IV CDK7 inhibitor that we had been developing in a Phase 1 clinical trial before we made the portfolio decision in October 2019 to discontinue its further development and prioritize the development of SY-5609. SY-5609 demonstrated approximately dose-proportional PK as both a single agent and in combination, minimal accumulation with repeat dosing, and a steady state half-life compatible with once-daily dosing. The majority of adverse events reported with SY-5609 as a single agent were low grade. The most common adverse events were nausea, diarrhea, fatigue, platelet count decrease, and vomiting. The safety profile of SY-5609 in combination with fulvestrant was consistent with that of single-agent SY-5609. Five of the 13 patients treated with single-agent SY-5609 were response evaluable, and of those, three achieved stable disease and two had progressive disease; one of the four patients treated in the combination cohort was response evaluable and had progressive disease. The maximum tolerated dose for continuous daily dosing was achieved at 3 mg. The Phase 1 clinical trial continues to actively enroll patients with select solid tumors, with additional cohort extensions in select populations. Alternate dosing regimens are also being explored in the trial. We expect to report additional dose escalation data, including clinical activity data, in the third quarter of 2021, and to initiate the expansion portion of the Phase 1 clinical trial in the second half of 2021.

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, license and collaboration agreements, and our term loan with Oxford Finance LLC, or Oxford. From inception through March 31, 2021, we raised an aggregate of $576.8 million from such transactions, including aggregate gross proceeds of $75.6 million through a public offering of our common stock in January 2021.

Since inception, we have incurred significant operating losses. Our net losses were $14.2 million and $17.2 million for the three months ended March 31, 2021 and 2020, respectively. As of March 31, 2021, we had an accumulated deficit of $391.2 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, SY-2101 and SY-5609;
- 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 research and preclinical programs;

- further develop our gene control platform;
- seek to identify and develop additional product candidates, which may involve entering into collaborations, licensing agreements or other arrangements;
- 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;
- become obligated to make milestone payments upon the successful completion of specified development and commercialization activities;
- 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
- add equipment and physical infrastructure to support our research and development programs.

Financial Operations Overview

Revenue

To date, our only 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 months ended March 31, 2021 and 2020, we recognized $4.8 million and $2.4 million of revenue, of which $4.0 million and $2.2 million was related to our collaboration with GBT and $0.8 million and $0.2 million to our collaboration with Incyte, respectively.

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 our 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 months ended March 31, 2021 and 2020 (in thousands):

	Three Months Ended March 31,	
	2021	2020
SY-1425 external costs	$ 4,512	$ 2,736
SY-5609 and other CDK7 program external costs (1)	3,106	2,715
SY-2101 program external costs	767	—
Other research and platform program external costs	3,351	2,358
Employee-related expenses, including stock-based compensation	6,710	5,255
Facilities and other expenses	1,583	1,505
Total research and development expenses	$ 20,029	$ 14,569

(1) Our SY-1365 clinical trial costs are included within this caption as part of our CDK7 programs. In October 2019 we announced our decision to discontinue further development of SY-1365, which was completed during the year ended December 31, 2020.

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;
- retention of key research and development personnel; and
- the impact of the COVID-19 pandemic.

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.

Interest Income

Interest income consists of interest income on our cash, cash equivalents, and investments in marketable securities, including the related amortization of premium and discounts.

Interest Expense

Interest expense consists of interest, amortization of debt discount, and amortization of deferred financing costs associated with our loans payable,and interest on finance lease arrangements.

Change in Fair Value of Warrant Liability

Change in fair value of warrant liability is the result of the remeasurement of the fair value of our warrant liability at each reporting period end.

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. There have been no significant changes to our critical

accounting policies discussed in our Annual Report on Form 10-K for the year ended December 31, 2020 that we filed with the SEC on March 4, 2021.

Results of Operations

Comparison of three months ended March 31, 2021 and 2020

The following table summarizes our results of operations for the three months ended March 31, 2021 and 2020, together with the changes in those items in dollars (in thousands):

	Three Months Ended March 31,			
	2021	2020	Dollar Change	% Change
Statements of Operations Data:				
Revenue	$ 4,827	$ 2,379	$ 2,448	103 %
Operating expenses:				
Research and development	20,029	14,569	5,460	37 %
General and administrative	5,739	5,149	590	11 %
Total operating expenses	25,768	19,718	6,050	31 %
Loss from operations	(20,941)	(17,339)	(3,602)	21 %
Interest income	10	384	(374)	(97) %
Interest expense	(967)	(271)	(696)	257 %
Change in fair value of warrant liability	7,670	—	7,670	100 %
Net loss	$ (14,228)	$ (17,226)	$ 2,998	(17) %

Revenue

For the three months ended March 31, 2021, revenue was $4.8 million, of which $4.0 million was attributable to our collaboration with GBT and $0.8 million was attributable to our collaboration with Incyte. For the three months ended March 31, 2020, revenue was $2.4 million, $2.2 million of which was attributable to our collaboration with GBT and $0.2 million was attributable to our collaboration with Incyte.

Research and Development Expense

Research and development expense increased by approximately $5.5 million, or 37%, from $14.6 million for the three months ended March 31, 2020 to $20.0 million for the three months ended March 31, 2021. The following table summarizes our research and development expenses for the three months ended March 31, 2021 and 2020, together with the changes to those items in dollars (in thousands):

	Three Months Ended March 31,			
	2021	2020	Dollar Change	% Change
External research and development	$ 10,806	$ 6,949	$ 3,857	56 %
Employee-related expenses, excluding stock-based compensation	5,386	4,205	1,181	28 %
Stock-based compensation	1,324	1,049	275	26 %
Consulting, licensing and professional fees	931	861	70	8 %
Facilities and other expenses	1,582	1,505	77	5 %
Total research and development expenses	$ 20,029	$ 14,569	$ 5,460	37 %

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

- an increase of approximately $3.9 million, or 56%, for external research and development costs, primarily due toincreases in costs associated with the continued advancement of our clinical programs, including the addition of SY-2101, and advancement of our preclinical programs, including our sickle cell disease development activities in collaboration with GBT;

- an increase of approximately $1.2 million, or 28%, for employee-related expenses, including increased salary and benefits, primarily due to our increased headcount; and
- an increase of approximately $0.3 million, or 26%, for stock-based compensation expense, also primarily due to our increased headcount.

General and Administrative Expense

General and administrative expense increased by approximately $0.6 million, or 11%, from $5.1 million for the three months ended March 31, 2020 to $5.7 million for the three months ended March 31, 2021. The change in general and administrative expense was primarily attributable to an increase in employee-related expenses driven by increased headcount, COVID-19 testing expenses incurred by us to support the health and safety of our lab-based employees, an increase in legal costs including patent registration fees and an increase in our information technology consulting costs incurred to enhance our processes and systems.

Interest Income

Interest income was derived generally from our investments in cash, cash equivalents and marketable securities. The decrease in interest income during the three months ended March 31, 2021 as compared to the three months ended March 31, 2020 was due to lower yield on our investments in cash and cash equivalents due to capital market conditions during the period ended March 31, 2021. We did not have investments in marketable securities during the three months ended March 31, 2021.

Interest Expense

Interest expense was related to our credit facility with Oxford and equipment financing arrangements. Interest expense increased by approximately $0.7 million, or 257%, from $0.3 million for the three months ended March 31, 2020 to $1.0 million for the three months ended March 31, 2021. The increase in interest expense during the three months ended March 31, 2021 as compared to the three months ended March 31, 2020 was driven by an increase in outstanding debt during the three months ended March 31, 2021 due to the drawing of a second tranche of $20.0 million from our credit facility with Oxford in December 2020, and therefore having two tranches of debt outstanding for the full three months ended March 31, 2021. Interest expense during the three months ended March 31, 2020 was based only on the first tranche of $20.0 million that was drawn in February 2020 and therefore was incurring interest expenses for only a part of the three months ended March 31, 2020.

Change in Fair Value of Warrant Liability

The change in fair value of warrant liability during the three months ended March 31, 2021 as compared to the three months ended March 31, 2020 was a result of the remeasurement of the fair value of warrants issued in connection with the private placement financing in December 2020.

Liquidity and Capital Resources

Sources of Liquidity

We funded our operations from inception through March 31, 2021, primarily through the sale of equity securities, through license and collaboration agreements, including those with Incyte and GBT, and through the credit facility with Oxford.

On February 12, 2020, we entered into a Loan and Security Agreement, or the Loan Agreement, with Oxford. Pursuant to the Loan Agreement, a term loan of up to an aggregate principal amount of $60.0 million is available to us. A $20.0 million term loan was funded on February 12, 2020, and another $20.0 million term loan was funded on December 23, 2020. As of March 31, 2021, $20.0 million remains available under the Loan Agreement at the sole discretion of Oxford.

On June 12, 2020, we filed a universal shelf registration statement on Form S-3 with the SEC to register for sale from time to time up to $300.0 million of common stock, preferred stock, debt securities, warrants and/or units in one or more registered offerings. The registration statement was declared effective on June 22, 2020. Further, in June 2020, we entered into an at-the-market sales agreement, or the 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 $75.0 million through Cowen pursuant to the registration statement. In January 2021, we issued shares of our common stock in an underwritten public offering resulting in gross proceeds of $75.6 million, before deducting underwriting discounts and commissions and other transaction expenses of approximately $5.1 million, pursuant to the Form S-3 that was filed with the SEC on June 12, 2020.

As of March 31, 2021, $75.0 million in common stock remained available for future issuance under the sales agreement.

As of March 31, 2021, $224.4 million of securities remained available for future issuance under the shelf registration statement.

As of March 31, 2021, we had cash and cash equivalents of approximately $222.1 million.

Cash Flows

The following table provides information regarding our cash flows for the three months ended March 31, 2021 and 2020 (in thousands):

	Three Months Ended March 31,	
	2021	2020
Net cash (used in) provided by:		
Operating activities	$ (21,990)	$ 246
Investing activities	(262)	43,203
Financing activities	70,410	31,693
Net increase in cash, cash equivalents and restricted cash	$ 48,158	$ 75,142

Net Cash (Used in) Provided by Operating Activities

The use of cash in the three months ended March 31, 2021 and cash provided by operating activities in the three months ended March 31, 2020 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 $22.0 million during the three months ended March 31, 2021 compared to net cash provided by operating activities of $0.2 million for the three months ended March 31, 2020. The increase in net cash used in operating activities during the three months ended March 31, 2021 was primarily due to a $3.6 million increase in loss from operations during the three months ended March 31, 2021 and the $20.0 million proceeds received in January 2020 from our collaboration agreement with GBT that was entered into in December 2019, which did not recur during the three months ended March 31, 2021.

Net Cash (Used in) Provided by Investing Activities

Net cash used in investing activities was $0.3 million during the three months ended March 31, 2021 compared to net cash provided by investing activities of $43.2 million during the three months ended March 31, 2020. The decrease in net cash provided by investing activities was primarily due to maturities of marketable securities of $45.0 million, offset by the $1.8 million purchase of property and equipment during the three months ended March 31, 2020, which did not recur during the three months ended March 31, 2021.

Net Cash Provided by Financing Activities

Net cash provided by financing activities was $70.4 million during the three months ended March 31, 2021 compared to net cash provided by financing activities of $31.7 million for the three months ended March 31, 2020. Cash provided by financing activities for the three months ended March 31, 2021 was primarily due to net proceeds of $70.4 million from a public offering of shares of our common stock, and $0.2 million of proceeds from the exercise of stock options, offset by $0.1 million of payments made under our finance lease. In comparison, the cash provided by financing activities for the three months ended March 31, 2020 was primarily due to $11.9 million of net proceeds from the issuance of shares of our common stock pursuant to the sales agreement, $19.7 million of net proceeds from the first tranche of the Oxford loan, and $0.1 million of proceeds from the exercise of stock options, offset by $0.1 million of payments made under our finance lease.

Funding Requirements

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue to advance our ongoing and planned clinical trials of SY-1425, SY-2101 and SY-5609, advance additional product candidates through research and 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. 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 and cash equivalents as of March 31, 2021, will enable us to fund our planned operating expense and capital expenditure requirements into 2023. 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, SY-2101 and SY-5609 and any associated companion diagnostic tests;
- 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 a drug candidate will be nominated to enter investigational new drug application-enabling studies under our sickle cell disease collaboration with GBT, whether GBT will exercise its option to exclusively license intellectual property arising from the collaboration, whether and when any option exercise fees, milestone payments or royalties under the collaboration agreement with GBT will ever be paid, and whether we exercise our U.S. co-promotion option under the GBT agreement;
- 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 gene control platform or to TMRC Co. Ltd., or TMRC, associated with the development, manufacture and commercialization of SY-1425;
- the timing and amount of milestone payments due to Orsenix associated with the development and commercialization of SY-2101;
- revenue received from commercial sales, if any, of our current and future product candidates;
- our headcount growth and associated costs as we advance our research and development programs 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 impact of the COVID-19 pandemic.

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, such as our term loan with Oxford, 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. In addition, the trading prices for our common stock has been and may continue to be highly volatile. As a result, we may face difficulties raising capital when needed through sales of our common stock or such sales may be on unfavorable terms.

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.

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 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 investment 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 March 31, 2021, we did not have significant 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 three-month periods ended March 31, 2021 and 2020.

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 officers, 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 March 31, 2021, 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

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, 2020, or the 2020 10-K. Any of the risk factors contained in this Quarterly Report on Form 10-Q and the 2020 10-K 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 the COVID-19 Pandemic

Public health epidemics or outbreaks, including COVID-19, have had, and will continue to have, an adverse impact on our business.

Public health crises such as pandemics or similar outbreaks could adversely impact our business. The novel strain of a virus named SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), or coronavirus, which causes coronavirus disease 2019, or COVID-19, has caused a pandemic that has reached multiple regions and countries, including Cambridge, Massachusetts where our primary office and laboratory space is located. The COVID-19 pandemic is evolving, and to date has led to the implementation of various responses, including government-imposed quarantines, travel restrictions and other public health safety measures, as well as reported adverse impacts on healthcare resources, facilities and providers, in Massachusetts, across the United States and in other countries. The extent to which COVID-19 continues to impact our operations or those of the third parties on which we rely will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the duration of the outbreak, additional or modified government actions, new information that will emerge concerning the severity and impact of COVID-19, and the actions to contain COVID-19 or address its impact in the short and long term.

Further, in response to the COVID-19 pandemic and in accordance with direction from state and local governmental authorities, we have restricted access to our facility to those individuals whose job responsibilities require or are significantly enhanced by on site presence, limited the number of people that can be present at our facility at any one time, and implemented a number of additional health and safety protocols. In the event that governmental authorities were to impose new restrictions, our employees conducting research and development activities may not be able to access our laboratory space, and our core research activities may be significantly limited or curtailed, possibly for an extended period of time. Sustained restrictions on our ability to conduct research would have an adverse impact on our ability to perform under our collaboration agreements with Global Blood Therapeutics, Inc. and Incyte Corporation, as well as delay the time in which we would be able to nominate new drug candidates for clinical development. In addition, it is possible that productivity and morale may be adversely impacted for those employees who are working remotely.

We believe that we have sufficient supply of clinical trial material to conduct our ongoing clinical trial activities, and we are implementing contingency plans to ensure that this continues to be the case. We source certain clinical trial material from contract manufacturing organizations in India, and we are assessing the potential impact of the recent surge of COVID-19 cases in India on our long-term supply chain needs. We cannot provide assurance that the COVID-19 pandemic will not delay or otherwise adversely affect our clinical development, research, manufacturing and business operations activities, as well as our business generally, in the future, which could have a material adverse impact on our operations and financial condition and results. These factors include:

- the impact on our clinical trial operations, including study start-up activities, of any diversion of healthcare resources away from the conduct of our ongoing or planned clinical trials in order to focus on pandemic concerns, including the availability of necessary materials, the attention of physicians serving as our clinical trial investigators, access to hospitals serving as our clinical trial sites, and availability of hospital staff supporting the conduct of our clinical trials;
- the impact on our clinical trials or our other development and regulatory objectives if we are unable to initiate sites or screen and enroll patients on the timelines that we originally anticipated, if we are unable to continue remote monitoring of clinical trial data or utilizing telehealth systems, local laboratory assessments and in-home nursing visits for enrolled patients, or if any patient enrolled in one of our clinical trials is unable to remain on study due to a COVID-19 diagnosis;

- potential interruptions in global shipping affecting the transport of clinical trial materials, such as investigational drug product, patient samples, and other supplies used in our clinical trials;

- the impact of further limitations on travel or working conditions that could interrupt key clinical trial activities, such as clinical trial site initiations and monitoring activities, travel by our employees, contractors or patients to clinical trial sites, or the ability of employees at any of our contract manufacturers or contract research organizations to report to work, any of which could delay or adversely impact the conduct or progress of our clinical trials and other research and manufacturing activities;

- any future interruption of, or delays in receiving, supplies of clinical trial material from our contract manufacturing organizations due to staffing shortages, production slowdowns or stoppages, or disruptions in delivery systems;

- availability of future capacity at our contract manufacturers to produce sufficient drug substance and drug product to meet forecasted clinical trial demand if any of these manufacturers elect or are required to divert attention or resources to the manufacture of other pharmaceutical products;

- delays in ongoing laboratory experiments and operations if we are required to reduce the number of employees in our laboratories, or if the contract research organizations we have retained to supplement our internal research efforts are unable to perform as anticipated, whether due to capacity constraints, staffing shortages, or otherwise; and

- business disruptions caused by potential workplace closures and an increased reliance on employees working from home, challenges in recruiting employees required to execute on our research and development plans, cybersecurity and data accessibility issues, and communication or transit disruptions, any of which could adversely impact our business operations and delay necessary interactions among our employees and between our company and the third parties upon which we rely.

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

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

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 several new drugs approved by the FDA since 2018 for the treatment of AML or patient subsets within AML (including ivosidenib, venetoclax, glasdegib and gilteritinib), and one new drug approved by the FDA in 2020 for the treatment of MDS or patient subsets within MDS (decitabine/cedazuridine). SY-1425 may also face competition from other investigational products currently in clinical development for AML and MDS, including investigational products in late-stage development from Takeda Pharmaceutical Co. Ltd., Daiichi Sankyo Company, Ltd., Servier Pharmaceuticals, LLC, Otsuka Pharmaceutical Co., Ltd., Roche Holding AG, Actinium Pharmaceuticals, Inc., GlycoMimetics, Inc., Arog Pharmaceuticals, Inc., Rafael Pharmaceuticals, Inc., argenx SE in collaboration with Janssen Pharmaceutica NV, Gilead Sciences, Inc., Geron Corporation, Delta-Fly Pharma, Inc., Aprea Therapeutics, Inc., SELLAS Life Sciences Group, Inc., Novartis AG, Astex Pharmaceuticals, Inc., and Bristol-Myers Squibb Co.

SY-2101 may face competition from Trisenox® or any of the generic forms of Trisenox, an intravenously administered arsenic trioxide product approved by the FDA for the treatment of APL. We are also aware of a traditional Chinese medicine (TCM)-based formulation of oral arsenic commercially available in China. In addition, we are aware of an oral formulation of arsenic trioxide in clinical development in Australia and New Zealand from the Australasian Leukemia and Lymphoma Group, and of an oral formulation of arsenic trioxide being studied in an academic setting in China.

In addition, we are aware of selective CDK7 inhibitors being developed in early clinical trials by Carrick Therapeutics Ltd., Eli Lilly & Co. and Exelixis, Inc., and three other selective CDK7 inhibitor programs that we believe are in preclinical development from Qurient Co. Ltd., Yungjin Pharma Co., Ltd., and The Translational Genomics Research Institute. SY-5609 may face competition from these CDK7 inhibitors. There is also significant competition from products with mechanisms other than CDK7 inhibition in the disease areas where we may choose to focus development of SY-5609 in the future. 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 competitors may 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.

Item 6. Exhibits.

Exhibit No.	Description of Exhibit
3.1	Restated Certificate of Incorporation of the Registrant, including the Certificate of Designation of Preferences, Rights and Limitation of Series A Convertible Preferred Stock of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended March 31, 2019 (File No. 001-37813) filed on May 1, 2019).
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).
10.1†	Amendment No. 1 to Amended and Restated Cancer License Agreement, dated January 8, 2021, by and between the Registrant and TMRC Co., Ltd. (filed herewith).
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	Inline XBRL Instance Document (the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document).
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Presentation Linkbase Document
104	Cover Page Interactive Data (formatted as Inline XBRL and contained in Exhibit 101)

† In accordance with Item 601(b)(10)(iv) of Regulation S-K, certain information (indicated by "[***]") has been excluded from this exhibit because it is both not material and would likely cause competitive harm to the Company if publicly disclosed.

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: May 6, 2021

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

Exhibit 10.1

CERTAIN IDENTIFIED INFORMATION HAS BEEN EXCLUDED FROM THIS EXHIBIT BECAUSE IT IS BOTH (I) NOT MATERIAL AND (II) WOULD BE COMPETITIVELY HARMFUL IF PUBLICLY DISCLOSED. SUCH EXCLUDED INFORMATION HAS BEEN MARKED WITH "[**]".

AMENDMENT NO. 1 TO AMENDED AND RESTATED CANCER LICENSE AGREEMENT

This Amendment to Amended and Restated License Agreement (this **"Amendment**") is made as of January 8, 2021 by and between Syros Pharmaceuticals, Inc., a Delaware corporation having a place of business at 35 CambridgePark Drive, 4th Floor, Cambridge, Massachusetts 02140 USA (**"Syros"**) TMRC Co., Ltd., a Japanese corporation having a place of business at 1-12-12, Kita Shinjuku, Shinjuku-ku, Tokyo 164-0074, Japan ("**TMRC**").

WHEREAS, TMRC and Syros entered an Amended and Restated Cancer License Agreement dated as of April 28, 2016 (the " **Agreement**");

WHEREAS, TMRC and Syros wish to amend the Agreement to (i) include additional Patent Rights Controlled by TMRC within the scope of the intellectual property licensed to Syros and (ii) expand the territory under which Syros is licensed to the Technology; and

WHEREAS, pursuant to Section 14.5 of the Agreement, the Agreement may be amended by a written instrument executed by the parties thereto.

NOW THEREFORE, for good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, TMRC and Syros each hereby agree as follows:

1. Amendments to Agreement. The Agreement is hereby amended as follows:

(a) The definition of "Territory" in Section 2.33 of the Agreement is hereby amended and restated as follows:

2.33 "Territory" means (a) North America (the United States of America, Canada, and Mexico); (b) Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Liechtenstein, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, Switzerland and the United Kingdom; (c) any other country to which the EMA's regulatory jurisdiction extends; (d) Central/South America (Argentina, Belize, Bolivia, Brazil, Chile, Colombia, Costa Rica, Ecuador, Guatemala, Guyana, Honduras, Nicaragua, Panama, Paraguay, Peru, Suriname, Uruguay and Venezuela); (e) Australia; (f) Russia; and (g) Israel.

(b) Exhibit A to the Agreement is hereby amended and restated in the form attached as Exhibit A hereto.

2. Miscellaneous. Except as expressly amended hereby, all other terms and conditions of the Agreement shall remain in full force and effect. Capitalized terms used in this Agreement that are not otherwise defined have the meanings given them in the Agreement. This Amendment shall be governed by and construed in accordance with the Laws of the State of California, without regard to the conflicts of law principles thereof. This Amendment may be executed in one or more counterparts, each of which shall be an original and all of which taken together shall constitute one and the same agreement. Signature pages to this Amendment may be exchanged by facsimile or electronically as a portable

document format (.pdf) file and such signature pages shall be deemed originals.

IN WITNESS WHEREOF, the parties hereto have executed this Amendment as of the date set forth above.

SYROS PHARMACEUTICALS, INC.		**TMRC CO., LTD.**	
By:	/s/ Nancy Simonian	By:	/s/ Naoki Tani
Name:	Nancy Simonian	Name:	Naoki Tani
Title:	President and Chief Executive Officer	Title:	President and Chief Executive Officer

EXHIBIT A

Certain Licensed Patent Rights

Series	Country or Region	Application No.	Filing Date	Publication	Patent	Priority	Subject Matter/Other Info
[**]	[**]	[**]	[**]	[**]	[**]	[**]	[**]
	[**]	[**]	[**]		[**]	[**]	[**]
	[**]	[**]	[**]		[**]	[**]	[**]
[**]	[**]	[**]	[**]	[**]	[**]	[**]	[**]
	[**]	[**]	[**]		[**]	[**]	[**]
	[**]	[**]	[**]		[**]	[**]	[**]
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	[**]	[**]	[**]	[**]		[**]	[**]
	[**]	[**]	[**]	[**]		[**]	[**]
	[**]		[**]	[**]		[**]	[**]
	[**]		[**]	[**]		[**]	[**]
	[**]	[**]	[**]	[**]		[**]	[**]

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 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 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: May 6, 2021

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 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 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: May 6, 2021

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 March 31, 2021 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 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of 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: May 6, 2021

/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 March 31, 2021 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 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of 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: May 6, 2021

/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.